



# THE YEAR BOOK *of* GENERAL SURGERY

(1956-1957 YEAR BOOK Series)

EDITED BY

EVARTS A. GRAHAM, A.B., M.D.

*Emeritus Professor of Surgery, Washington University School of  
Medicine; formerly Surgeon in Chief of the Barnes Hospital  
and of the Children's Hospital, St. Louis*

With a Section on  
ANESTHESIA

EDITED BY

STUART C. CULLEN, M.D.

*Professor of Surgery and Chairman of Division of Anesthesiology  
State University of Iowa College of Medicine  
and Hospitals*

## THE YEAR BOOK PUBLISHERS

INCORPORATED

200 EAST ILLINOIS STREET

CHICAGO 11



## TABLE OF CONTENTS

**PUBLISHER'S NOTE** The designation (Series 1956-1957) used on the cover and title page of this volume is to indicate its publication during the series year which begins September 1956 with the publication of the YEAR BOOK OF MEDICINE and ends in May 1957 with the YEAR BOOK OF PATHOLOGY AND CLINICAL PATHOLOGY

The articles abstracted herein are taken from journals received between April 1955 and May 1956

Introduction	5
General Considerations	9
Technical Contributions	43
Nutrition	55
Shock Fluids and Electrolytes	59
Wounds and Wound Healing	72
Antibiotics	79
Neoplasms	81
The Head	108
The Neck	113
The Thyroid	115
The Breast	133
The Lungs and Pleura	161
The Thorax and Mediastinum	226
The Heart	234
The Aorta and Peripheral Arteries	292
Peripheral Veins	321
Lymphatic System	328
Abdomen—General	335
The Liver and Spleen	340
The Biliary Tract	362
The Pancreas	383
The Esophagus	397
The Stomach and Duodenum	417



## TABLE OF CONTENTS

The Small Intestine	450
The Appendix	461
The Colon and Rectum	466
Pilonidal Cysts and Sinuses	493
Hernia	497
The Adrenal Glands	502
The Genitourinary System	510
The Extremities	511

## ANESTHESIA

Depressant Drugs	537
Ventilation	554
Inhalation Anesthesia	568
Muscle Relaxants	572
Barbiturates	576
Spinal Anesthesia	580
Regional Anesthesia	589
Hypothermia	593
Circulation	599
Miscellaneous	616

## INTRODUCTION

Have we been mistaken for about three quarters of a century in some of our basic concepts of the treatment of cancer? Is it possible that we could have been as wrong as many recent articles would imply? Some of the concepts that have generally been regarded as basic in the application of surgery to the treatment of cancer follow. (1) Wide excision of the malignant lesion, together with the lymphatic vessels and nodes that receive and transmit the cancer, will give a better ultimate result than a less extensive operative procedure. (2) Early operation is greatly to be desired. (3) A single so-called recurrence or metastasis, if accessible, should be removed. (4) For most cancers, surgical extirpation gives better results than any other treatment known at present.

Now along comes N. E. McKinnon (abstracted in the section on the Breast), of the University of Toronto, not a surgeon but a statistician and epidemiologist, who tells the Canadian Medical Association that "aggressive programmes over the past 25-30 years for the control of cancer mortality, and more particularly that of breast cancer, have failed to make any impression on the latter recorded mortality." Again he states that, "the evidence that treatment of breast cancer prevents death in a very considerable proportion of cases or that early treatment is greatly superior in this regard must be rejected because it is based for the most part on invalid comparisons of survival rates." Similarly Denoix, of Paris (abstracted in the section on Neoplasms), on the basis of a study of 13,291 cases of cancer of the breast, uterus, tongue, skin and larynx states that the prognosis of cancer of the cervix remained practically the same regardless of the time of treatment. He thinks, however, that probably, although he is not sure, in certain types of breast cancer early treatment is seen to have a more favorable effect. Crile, in his book published last year (*Cancer and Common Sense* [New York: Viking Press, 1955]) also developed the point that the time of treatment of the cancer is probably not so important as we have thought it to be, for the reasons that we do not know anyway in a particular

case how long the cancer has been present when it is first detected, nor do we know the virulence of the cancer or whether distant metastases are already present. Gatch, in an article that was commented on last year in the Introduction to the YEAR BOOK, states that the concept that block dissection with wide removal of local tissues and regional lymphatics is based on the probably erroneous idea of Halsted and Handley that cancer spreads from a focus along the lymphatic vessels in solid unbroken cords and that the surgeon's task is to get beyond the periphery of the cancer sheet. Gatch thinks that in many more cases than we suppose there are already blood-borne distant metastases at the time of operation, and he casts doubt on the validity of Halsted's idea. It is interesting that at one time he was a resident of Halsted's at the Johns Hopkins Hospital.

Lewison in a recent article (abstracted in the section on the Breast) reproduces a chart prepared by the World Health Organization that shows the increasing mortality rate of women with cancer of the breast in England and Wales, Scotland, Australia, Denmark, The Netherlands and Switzerland. It is distressing to find the mortality increasing despite the fact that undoubtedly there have been in recent years more excellent surgeons available in those countries than ever before, who have the knowledge and the equipment to give their patients the best that surgery can offer. One may perhaps find scant comfort in the fact that now there are many more women of the cancer age, who, if they happen to get cancer of the breast and are operated on, may die with metastases before a five year postoperative period has elapsed. Such occurrences will increase the mortality rate of cancer of the breast. Yet we can hardly explain on such weak arguments the failure to make a better showing with our modern surgical treatment.

McWhirter, a radiotherapist at the Edinburgh Royal Infirmary, has convinced many in Great Britain that the best course of treatment for cancer of the breast is simple mastectomy followed by intensive x-ray therapy. His reputation has spread to this country, with the result that not only physicians but sometimes even patients inquire about his plan of treatment. Fortunately, an opportunity to go to Edinburgh to make a thorough study and appraisal of the

method was extended by Dr McWhirter to Lauren Ackerman, in charge of the section of surgical pathology at Washington University. His article (abstracted in the section on the Breast) will be interesting to those who wish to know more about the results of the method. Ackerman found many weaknesses in the compilation of results, and he was by no means convinced that McWhirter's method should supersede radical operation (such as Halsted's) by a well trained and competent surgeon.

I have limited my remarks here to cancer of the breast because that condition has perhaps been as well studied as any other cancer and there has been an excellent opportunity for many years to observe the effects of surgical and other forms of treatment. But where does all this discussion leave us? I confess I do not know. At present it is certainly too early to abandon a well planned operation, especially when it can be performed in what seems to be a fairly early case. Yet alert surgeons must realize that recent evidence, some of which I have presented here, would indicate that we must give a second look to the question of whether we are on the right track in having as much confidence in surgical treatment of cancer of the breast as we have now.

—EVARTS A GRAHAM



## GENERAL CONSIDERATIONS

**Crash and Live—Need Cars Kill More Soldiers Than Guns?** Don S. Wenger<sup>1</sup> (USAF) states that the automobile is the military establishment's and the nation's greatest killer. An American is injured every 24 seconds and one is killed every 14 minutes in a traffic accident. Adjusted for male groups of comparable ages, the military service has about 30% more fatalities due to auto accidents than do civilians. Most deaths and injuries in auto accidents are due to decelerative forces that bring the occupant against solid objects. The body is well able to withstand the decelerative forces in most auto accidents without injury. Improved engineering and support and restraints of the body will sharply reduce auto accident fatalities.

The doors and framework are the most lethal parts of a car. A close second are objects outside the car against which the ejected occupant is thrown. Regardless of the severity of the accidents, more occupants sustain injuries by being ejected than by remaining in the car. Second to minor injuries, head injuries are commonest.

Prevention of injuries and deaths is simple. If high peaks of decelerative forces were reduced, if areas that absorb these forces were enlarged and if the occupants were restrained so that they would not fly around inside or outside the car, most fatalities and injuries would never occur. Possible mechanisms for obtaining these results are safety belts, a progressively disintegrating frame and energy-absorbing construction of various lethal parts of the vehicle, such as steering wheels, instrument panels, windshields and seat backs. A shock absorbing bumper, either hydraulic or collapsible, padded panels and pop out windshields are possible examples of such construction. A high backed seat would materially reduce whiplash neck injuries. If properly packaged for survival, a person can crash a car and still live.

► [Are we ever going to do anything decisive about the automobile's propensities for murder and injury? What is the use of getting excited about

wonder how we could permit an agent of death of 200 or more horsepower, that can go at 100 miles per hour, roam around our city streets. Is it necessary? Of course not. In most accidents speed is an important factor. If we really cared about the slaughter we would demand that no car be allowed to be sold that would go faster than say, 50 miles per hour. Think of it! A million injuries a year, many of them permanent!

Dr. Wenger's suggestions about making a crash less serious are excellent but of course they do not really hit the bull's eye because they do nothing to control the speed of the car. When are we going to do something fundamental?—Ed.]

**Asepsis and Antisepsis of surgical wounds** is discussed by Harold A. Zintel<sup>2</sup> (Columbia Univ.), in the light of present knowledge of wound healing.

1 Preparation of surgeon's hands—Hexachlorophene, bis(2-hydroxy-2,5,6 trichlorophenyl) methane, is the first antiseptic which remains effective in combination with soap. Hexachlorophene preparations are available in both liquid and solid (bar) forms. The most effective is one using 3% hexachlorophene in a detergent (pHisoHex®). This preparation allows a three minute initial scrub and a one minute scrub between operations, regardless of how often the surgeon operates. The scrubbing technic follows. After rinsing hands and arms with running tap water, 2 cc of preparation is applied to remain in contact with skin for one minute while fingernails are cleaned with a sterile nail stick. Detergent preparation is then rinsed off with tap water. Following a second 2 cc application, skin is scrubbed with a brush for two minutes. Hands and arms are then rinsed with tap water and dried with a sterile towel. An antiseptic hand dip is not required as it does not produce further degermation and alcohol inactivates the hexachlorophene deposited on the skin. After one week's use and also after one year's use of detergent hexachlorophene, postscrub bacteria count is 24% of prescrub bacteria count before initial use of the preparation.

2 Preparation of patient's skin—Although countless antiseptics have been extensively used for preoperative preparation none has proved definitely superior to a 70% alcohol solution and none reasonably approaches the effectiveness of 2% tincture of iodine or the five cup preparation. The detergent hexachlorophene preparation is not a superior agent for skin preparation. Several studies have shown no difference in incidence of wound infections or

(2) S. Clin. North America 36:257-271 April 1956

variable bacteria when wound covers were used or when they were not

3 Sterilization—All surgical equipment not seriously affected by heat, including syringes and needles, should be sterilized by autoclaving. Sharp and certain other delicate instruments should be immersed for an adequate period in an antiseptic solution, e.g., formaldehyde solution USP, 130 Gm, potassium nitrite, 0.15 Gm, sodium hydroxide, 0.012 Gm, hexachlorophene (G-11), 5 Gm, with ethyl alcohol (95% CP) to make 1 000 cc. This will kill vegetative bacteria in 20 minutes and spores in 3 hours. Zephiran® is a less effective preparation because it requires 18 instead of 3 hours. Bichloride of mercury, merthiolate,® metaphen,® mercresin,® mercurochrome,® mercury chloride and the phenols and cresols are unsuitable because they have no sporicidal effect. Instruments containing shellac, plastics, lenses and electrical connections must be sterilized by formaldehyde gas or immersed in an aqueous germicide such as zephiran® (for 18 hours). Alcohol solutions cannot be used. Hot air or radiant heat sterilization is indicated for ophthalmic instruments, because minute amounts of chemicals not removed by rinsing are deleterious to eye tissues. A radiant energy sterilizer (Wilmot-Castle), provides heat of 160 C for one hour, this is an overnight method.

4 Wounds—Presence or absence of wound infection is determined entirely on the basis of clinical findings. Purulent drainage is suggestive, but not diagnostic of such infection. True wound infection is diagnosed on the basis of one or more of the following: (1) excessive inflammation—swelling, redness, local heat, pain and tenderness, (2) tissue necrosis and/or (3) excessive systemic response, such as variations in temperature, pulse, respiration, leukocytosis, sensorium and function.

Any antiseptic agent capable of killing bacteria is also capable of killing living tissue cells. Hence, an antiseptic should never be applied to the surface of wound, but should be restricted to surrounding skin surface. Military experience showed that when a wound appeared surgically clean—free from necrotic material and with its surface showing clean granulation tissue—it was ready for closure, regardless of number or type of bacteria that could be cultured from its surface.



Despite voluminous literature on the presumed usefulness of topically applied antibiotics, no scientific data are known that prove their value in man. Careful, thorough debridement is the best method to free a wound from necrotic tissue. Closure will be immediate, 4-10 days later (early secondary or late primary) or late, i.e., 10 or more days after debridement.

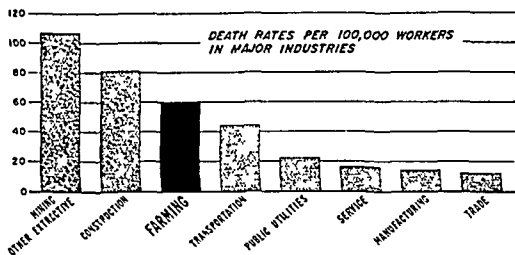
Prophylactic use of antibiotics systemically should be restricted to patients who have (1) traumatic wounds resulting from violence, including burns, (2) clean contaminated wounds produced by operations, e.g., of gastrointestinal, urinary and respiratory tracts, (3) emergency surgery in presence of infection, e.g., pharyngitis, (4) pre-existing valvular heart disease, (5) any urinary tract derangements, including kidney stones, or even an indwelling catheter, and (6) opening of the thoracic cavity. There is no justification for prophylactic antibiotic therapy in patients with clean, uncontaminated wounds resulting from elective surgery, e.g., breast biopsy or herniorrhaphy. Dangers in indiscriminate use of antibiotics include sensitization of an alarming number of patients and increased resistance of environmental bacteria. Besides, the added cost to the patient is not inconsiderable.

The most generally effective combination of antibiotics, when indicated in surgical cases, is penicillin 400,000 units, and streptomycin, 0.5 Gm, intramuscularly every 12 hours. This combination is available commercially as combiotic® or dicrysticin®. Wide spectrum antibiotics such as tetracycline, chloramphenicol, erythromycin and oxytetracycline can be substituted for streptomycin. Oral preparations should be used as soon as the patient is able to absorb medication by this route. All patients in shock or likely to go into shock should receive massive intravenous doses of penicillin, 500,000-1,000,000 units, before operation. Streptomycin cannot be given intravenously, but other preparations can be given in 500 mg doses. As soon as danger of shock has subsided, intramuscular antibiotic therapy should be used. Prophylactic therapy should be discontinued in five to seven days. In treatment of infections, therapy can be discontinued when the patient is clinically recovered and temperature is normal for 48 hours. If acute infections do not respond within five days, antibiotic therapy should be

altered according to new cultures and sensitivity tests and search should be made for localized abscesses. Initial antibiotic therapy is empiric.

**Farm Injuries.** Farm work accounts for about a fourth of all deaths on the job in the United States, and over 1,000,000 nonfatal farm accidents occur annually. Annual death rate/100,000 workers (Fig. 1) is about 60. Howard E. Snyder<sup>3</sup> (Winfield, Kan.) notes that the Kansas death rate, 1950-54, was only 32/100,000. This is attributed partly to

## Farming vs other industries



COURTESY KANSAS STATE BOARD OF HEALTH

Fig 1—Accident death rates in major industries in the United States in 1953 (Courtesy of Snyder, H E South M J 49 387 393, April, 1956)

the safety program inaugurated by the State Board of Health and other agencies. In 1954, 50 farm work deaths (all-time low) comprised 35% of accident fatalities in all industries in Kansas.

Wounds and injuries incurred on the farm include fractures, sprains, lacerations, contusions, burns, severe injuries from blunt agents, with rupture of solid or hollow abdominal organs, crushing injuries of the chest and severely lacerated, contused and contaminated wounds. The general practitioner or general surgeon is most often called upon to care for these injuries. He must recognize and treat shock promptly and accurately and appraise extent and character of wounds. If rupture of a viscus is suspected, immediate exploratory surgery is indicated. Negative results of peri-

(3) South M J 49 387 393, April 1956

toneal tap or x-ray should not delay surgery if other indications are present. Severely lacerated, mangled and contaminated wounds must have thorough debridement and should not be closed primarily when they involve muscular parts of an extremity.

Debridement of a large wound, e g, in the thigh (Fig 2), requires enlargement by incisions, permitting adequate exploration of deep tissues. Placing longitudinal skin incisions on a different plane at the superior and inferior aspects of

## DÉBRIDEMENT

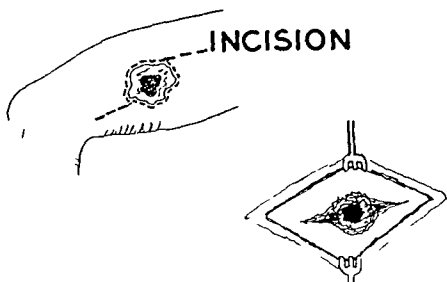


Fig 2—Wound in thigh enlarged by incisions (Courtesy of Snyder, H. E. South M J 49 387 393, April, 1956)

the primary wound facilitates closure by delayed or primary suture because it employs principles of Z-plasty used by the plastic surgeon. A thin rind of skin, including impregnated dirt, should be excised from the edges of the wound, but skin should not be needlessly sacrificed. Longitudinal incisions in the fascia above and below the wound permit adequate debridement of underlying tissues. All devitalized fascia and all muscle that does not bleed when cut or contract when pinched should be excised. Completely detached bone fragments should be removed. Bone with remaining periosteal attachment should be left. All foreign bodies and dirt must be removed, and the wound should be irrigated with copious normal salt solution. If the wound is perforating, similar incisions should be made at the entrance and

**CLOSURE** If the wound is badly contaminated or was incurred over four hours before operation, it must not be closed primarily. After adequate excision or debridement, fine mesh gauze is laid in the wound and covered with flat pieces of surgical gauze and absorbent pads, supplemented with a plaster cast or splint if indicated. A wound so dressed can be left four to eight days. Then if the wound is clean and no dead tissue remains, it may be safely closed by suture or by split thickness skin grafts. If remaining dead tissue can be completely excised, the wound may be closed after the secondary debridement. If there is invasive infection, the wound should be left open and treated with wet dressings and appropriate antibiotics. Closure is delayed until all evidence of infection has disappeared.

A few wounds, such as those of joints and skull, and sucking wounds of the chest should be closed primarily. Wounds of the hand, with exposed tendons and nerves, demand partial early closure. When a flap of skin has been denuded from the back of the hand, a few interrupted sutures, widely spaced, may suffice. Even in wounds of soft parts of extremities (usually left open), if a nerve or important blood vessel is exposed, slight closure by approximation of overlying muscle is indicated.

Immunization against tetanus and gas gangrene must be considered in all wounds incurred on a farm. Tetanus antitoxin should be given to those who have never had tetanus toxoid immunization. The usual 1,500 unit dose of antitoxin should be doubled for every day that administration is delayed beyond wounding. In a contaminated wound over 24 hours old, 10,000 units of antitoxin should probably be used. Those who have received tetanus toxoid within four years are adequately protected if they are given a booster dose of toxoid. It is wise to use antitoxin and a booster dose of toxoid—in separate syringes and separate arms—in those who received the last booster dose more than four years before injury.

Gas gangrene antitoxin is of no value in prophylaxis of gas gangrene. Adequate debridement with delayed suture of the wounds is the best protection. Localized anaerobic infection due to clostridia (anaerobic cellulitis) must be differentiated from true gas gangrene. In such cases there may be gas bubbling from a wound, a foul odor and a gray

ough of devitalized tissue in the wound base, but if this devitalized tissue is excised, live healthy bleeding muscle is encountered. This is the real distinguishing point in differentiation of anaerobic cellulitis and true gas gangrene. Organisms resembling clostridia in direct smears from wounds or a blob of air on an x-ray film do not establish diagnosis of gas gangrene. A patient with gas gangrene will be sick, have acceleration of pulse disproportionate to fever and be apprehensive. A patient with anaerobic cellulitis may have slight fever, but the pulse is not unduly elevated.

[Except for the greater tendency to develop anaerobic infections, farm injuries are not especially different from others. There is, however, perhaps a greater delay in getting medical care than, for example, in industrial accidents. Infection therefore, may be more pronounced—Ed.]

**Some Common Mishaps** are discussed by Norman C. Lake<sup>4</sup> (Charing Cross Hosp., London). Splinters under a nail are easily removed with forceps, and the nail does not have to be dressed. Subungual hematomas near the end of the nail can be evacuated by lifting the end of the nail with a knife, but those further back are evacuated by boring a hole in the nail over the blood. Mallet finger is treated by flexing the intermediate joint and hyperextending the terminal joint and then splinting the finger for five weeks. Impacted rings are treated by wrapping the finger with dress-maker's tape to reduce the edema, then pulling the end of the tape under the ring, using a wire loop slipped between ring and finger. After soaping, a steady pull on the tape will slowly spiral the ring off (Fig. 3). Some impacted rings must be cut off.

Cuts, especially on the fingers, caused by meat or fish knives can cause erysipeloid of Rosenbach and should be treated with penicillin. In cuts, lacerations and abrasions of the face the tattooing of dust, coal and tar must be avoided by picking the large pieces out with forceps. The smaller pieces can be removed by washing with detergent, chloroethylene or soap. Small lacerations can be closed with adhesive strips. Human and dog bites must be treated with antitetanus serum. Insect stings should be treated with antihistamines.

Penetrating foreign bodies can be located by palpation or x-ray. Small foreign bodies can often be removed by enlarging the wound of entry and withdrawing them with

forceps. Fluoroscopy aids in removal of some foreign bodies. If the point of an indelible pencil becomes imbedded in the skin, the whole area stained by the dye and the pencil tip should be excised. A penetrating fishhook should be pushed in until the point penetrates the skin from within, the point cut off and the hook withdrawn along its original track.

Swallowed foreign bodies occasionally have to be removed. Impacted foreign bodies in the ears can be syringed or suctioned out. Paraphimosis can be reduced by backward pressure on the glans or injection of 500-1,000 units

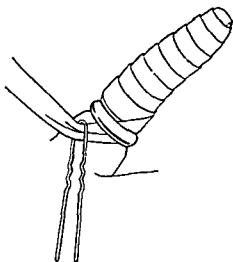


Fig. 3—Removing impacted ring from finger with a spiral of dressmaker's tape (Courtesy of Lake N. C. Brit. M. J. 2 1550 1552 Dec. 24, 1955)

of hyaluronidase into the swelling. Anal impactions often must be broken up by the gloved finger. Occasionally warm olive oil or medicinal paraffin aids evacuation of inspissated feces. A thrombosed external pile should be treated by a small radial incision to evacuate the clot. A prolapsed internal pile can occasionally be reduced. Prolapse of the rectum in children is not serious and can be treated by reducing the prolapse and strapping the buttocks together. Injection of about 3 ml. phenol in almond oil into the submucosa at three points around its circumference helps prevent recurrence. An acute painful fissure at the posterior anal margin can be treated by application of an analgesic ointment and dilatation of the anal canal. Proctalgia fugax can be relieved by the patient himself by insertion of a

finger, passage of flatus or by injection of air through a Higginson syringe

► [Too often young surgeons who are able to take care of major cases are at sea when confronted with some of the minor problems mentioned here by Lake. It seems fitting therefore, to give some space to a discussion of some of the mishaps—Ed.]

**Traumatic Fat Necrosis**, although often overlooked, is a relatively common lesion, according to Brooke Roberts, Robert Reed and William T. Fitts, Jr.,<sup>5</sup> who report 163 cases observed at the hospital of the University of Pennsylvania in 12 years. All cases associated with pancreatitis were excluded. The lesion was in the breast in 74, in or about the peritoneal cavity in 64 and in subcutaneous tissue in 25. Fat necrosis occurs predominantly in females (84% in this series). In 50%, lesions were associated with previous trauma, in 10%, with incarceration or strangulation of tissue, and in 14%, with infection. Fat necroses in the peritoneal cavity were in the omentum in 23, in the peritoneum or preperitoneal fat in 16 and in bowel mesentery in 14. The rest were in various areas—gallbladder, epiploic appendages and mesosalpinx. Trauma was a factor in 58% of the abdominal cases. Fat necrosis involving subcutaneous tissues exclusive of the breast was scattered widely over the body and resulted from various causes. Trauma was responsible in over half. One lesion attributed to radiation was in the abdominal wall of a patient who had received irradiation for carcinoma of the cervix nine months previously. Fat necrosis developed in a newborn baby in the preauricular region where forceps had been applied at delivery. Five cases were found in lipomas.

In many instances, fat necrosis resolves itself, particularly in young children. When the lesion is palpable, it is readily confused with neoplastic growths. Surgeons must keep this entity in mind to avoid some serious errors. Fat necrosis of the breast, particularly, can closely simulate cancer on preoperative examination.

History of injections or other trauma is helpful in making a differential diagnosis, although surgical excision may be necessary if fat necrosis does not subside. Injuries to lower extremities may be associated with traumatic fat necrosis which may not resolve for long periods. This is especially true in obese women with varicose veins in whom trauma

to the legs may be followed by indolent ulcers and painful indurated areas of fat necrosis

► [Traumatic fat necrosis of the breast was first described by Lee and Adair in 1920. Many cases have been described since then. The similarity of the lesion to carcinoma on gross examination has been repeatedly emphasized but it is well to call attention to it again. Twenty years ago it was probably seen more often when hypodermoclysis was used more commonly than today. Sometimes the needles were inserted by accident into the breasts instead of under them with the result that enough pressure was built up in them to cause necrosis of some of the fat—Ed.]

**Experimental Study of the Etiology of Fat Embolism** was made by W. W. Gies (Eloise, Mich.), T. D. Grekin (Royal Oak, Mich.), H. L. Davis (Omaha) and M. M. Musselman (Omaha). According to one theory of the causation of fat embolism, fat may be liberated at the site of trauma and gain access to open veins; the humoral theory postulates that fatty emboli may come from the physiologic emulsion of fat normally circulating in the blood. A third possibility is that a trigger mechanism causes agglomeration of the particles of fat in the blood.

Injection of fat from the marrow of the femur of rabbits into the ear vein of other rabbits of equal size resulted in death in 9 of 10 animals. Injection of an equal amount of corn oil resulted in no deaths. Severe fat embolism of the lungs was found 24 hours after fracture of both femurs. In animals killed immediately after fracture about the same amount of fat embolism was found. Removal of the adrenals did not prevent fat embolism. Significant fat embolism did not occur from administration of corticotropin or cortisone. Less fat embolism was found in rabbits in which embolism was induced by femoral fractures while the animals were in shock. Large amounts of stained fat appeared in the lungs after fracture of femurs into which stained fat had been introduced, less with hydrogenated cottonseed oil than with corn oil. Heparin increased rather than decreased the mortality from fat embolism.

The study demonstrated no evidence of the humoral or trigger theory of fat embolism. Mechanical fat embolism did occur under the conditions of the experiments.

► [Of course the necessary condition is that the fat globules that get into the blood stream be larger than the blood corpuscles. A discussion of the amount of fat in the blood is beside the point. Severe lipemia may exist without embolism—Ed.]



**Use of Blood and Plasma in Surgical Practice** According to J Garrott Allen and Edward A Stemmer<sup>7</sup> (Univ of Chicago), blood transfusion is used principally for prevention and treatment of hypovolemic shock, correction of anemia when other measures will not serve equally well or better and in partial or complete exchange transfusions, as in erythroblastosis fetalis and monoxide poisoning Plasma is used in preference to blood in shock resulting from burns and peritonitis and in correction of hypoproteinemia in patients unable to eat Plasma is also useful as a standby or emergency fluid in treatment of hypovolemic shock until blood can be prepared Blood and plasma have specific advantages and risks, and proper choice between them and water and saline solutions is not always simple The following outline stressing the nature of the fluid disorder responsible for hypovolemia is useful, even though often more than one fluid has been lost

Hypovolemic hypotension due to *blood loss* may be (1) external, as in lacerations or bleeding ulcer, or (2) internal as in femoral fracture, crushing injury or ruptured spleen *Plasma loss* may be (1) external, as in burns, in which blood also may be lost, (2) internal, as in peritonitis, or (3) due to crushing injury, when generally more blood is lost than plasma In *water deprivation* electrolytes are concentrated and not lost and indicated therapy is water without salt In *water loss*, as from vomiting high intestinal pancreatic or biliary fistulas and diarrhea generally electrolytes also are lost and water with electrolytes is needed

To estimate quantity of blood lost in surgical cases sponges and lap pads may be weighed A simpler method recommended by the authors is sponge and lap pad counts Approximate values for  $4 \times 8$  in sponges and  $6 \times 18$  in cotton lap pads are 10 cc and 100 cc, respectively Both weighing and counting of sponges have their greatest value in constantly reminding the surgeon that blood is being lost

Three guides are useful in evaluating type and volume of fluid a burned patient should receive (1) extent of surface area burned (2) hourly urinary excretion and (3) patient's response to treatment If he remains in shock, more blood and plasma are indicated particularly if hemoconcentration is present If he becomes edematous, fluid and salt restric

tion may be necessary. Most patients whose burned surface area is under 15% require little or no parenteral fluid, but in elderly patients, some fluids should be given if burned area exceeds 10%. Total amount of fluid administered to burned patients during the first 24 hours is calculated by multiplying body weight in kilograms by percentage of skin area burned, times three. Thus, for a 70 kg man with a 35% burn, anticipated fluid requirement for first day is 7,350 cc, of which 3,675 (50%) should be colloid-bearing solutions, including blood, and 25%, or 1,840 cc, of 5% dextrose in water. Volume of fluids taken by mouth is deducted from calculated intravenous water requirement. If no fluid can be taken orally, 25% of the total is given as normal saline solution. The second day, volumes of all fluids are reduced by half. After the second day, parenteral fluids are seldom necessary, unless facial burns prevent eating and drinking. After 48 hours, salt intake is restricted to no more than 5 Gm/day, preferably less. Normal salt intake may be resumed at end of a week or 10 days.

In treatment of hypoproteinemia in patients who cannot take food by mouth, daily transfusion of a liter or more of plasma will elevate concentration of plasma proteins in three to six days. Smaller quantities are likely to have little effect in the depleted patient. Administration of 500 cc blood between transfusion of each liter of plasma corrects anemia and permits the patient to come to operation with normal concentration of both hemoglobin and plasma proteins. Postoperative administration of blood and/or plasma is continued until he is able to eat, but usually smaller volumes are required. The value of plasma as a source of protein was proved experimentally in puppies, taking a protein-free diet, that flourished on plasma in contrast to litter mates that received amino acid hydrolysate intravenously or no protein.

Chief transfusion hazards are mismatching and typing errors, hepatitis (which can be controlled by storing plasma at room temperature six months or longer), citrate intoxication and bacterial contamination and potassium intoxication (which can be avoided by using blood within 10 days).

► [In these days when large quantities of blood and plasma are used it is important to realize that the danger of causing hepatitis has been practically eliminated by Dr. Allen's discovery that the simple device of stor-

Use of Blood and Plasma in Surgical Practice According to J Garrott Allen and Edward A Stemmer<sup>7</sup> (Univ of Chicago), blood transfusion is used principally for prevention and treatment of hypovolemic shock, correction of anemia when other measures will not serve equally well or better and in partial or complete exchange transfusions, as in erythroblastosis fetalis and monoxide poisoning Plasma is used in preference to blood in shock resulting from burns and peritonitis and in correction of hypoproteinemia in patients unable to eat Plasma is also useful as a standby or emergency fluid in treatment of hypovolemic shock until blood can be prepared Blood and plasma have specific advantages and risks, and proper choice between them and water and saline solutions is not always simple The following outline stressing the nature of the fluid disorder responsible for hypovolemia is useful, even though often more than one fluid has been lost

Hypovolemic hypotension due to *blood loss* may be (1) external, as in lacerations or bleeding ulcer, or (2) internal, as in femoral fracture, crushing injury or ruptured spleen *Plasma loss* may be (1) external, as in burns, in which blood also may be lost, (2) internal, as in peritonitis, or (3) due to crushing injury, when generally more blood is lost than plasma In *water deprivation* electrolytes are concentrated and not lost and indicated therapy is water without salt In *water loss*, as from vomiting high intestinal pancreatic or biliary fistulas and diarrhea generally electrolytes also are lost and water with electrolytes is needed

To estimate quantity of blood lost in surgical cases sponges and lap pads may be weighed A simpler method recommended by the authors is sponge and lap pad counts Approximate values for  $4 \times 8$  in sponges and  $6 \times 18$  in cotton lap pads are 10 cc and 100 cc, respectively Both weighing and counting of sponges have their greatest value in constantly reminding the surgeon that blood is being lost

Three guides are useful in evaluating type and volume of fluid a burned patient should receive (1) extent of surface area burned (2) hourly urinary excretion and (3) patient's response to treatment If he remains in shock, more blood and plasma are indicated particularly if hemoconcentration is present If he becomes edematous fluid and salt restric

(7) S Clin. North America 35 1597 1611 December 1955

tion may be necessary. Most patients whose burned surface area is under 15% require little or no parenteral fluid, but in elderly patients, some fluids should be given if burned area exceeds 10%. Total amount of fluid administered to burned patients during the first 24 hours is calculated by multiplying body weight in kilograms by percentage of skin area burned, times three. Thus, for a 70 kg man with a 35% burn, anticipated fluid requirement for first day is 7,350 cc, of which 3,675 (50%) should be colloid bearing solutions, including blood, and 25%, or 1,840 cc, of 5% dextrose in water. Volume of fluids taken by mouth is deducted from calculated intravenous water requirement. If no fluid can be taken orally, 25% of the total is given as normal saline solution. The second day, volumes of all fluids are reduced by half. After the second day, parenteral fluids are seldom necessary, unless facial burns prevent eating and drinking. After 48 hours, salt intake is restricted to no more than 5 Gm/day, preferably less. Normal salt intake may be resumed at end of a week or 10 days.

In treatment of hypoproteinemia in patients who cannot take food by mouth, daily transfusion of a liter or more of plasma will elevate concentration of plasma proteins in three to six days. Smaller quantities are likely to have little effect in the depleted patient. Administration of 500 cc blood between transfusion of each liter of plasma corrects anemia and permits the patient to come to operation with normal concentration of both hemoglobin and plasma proteins. Postoperative administration of blood and/or plasma is continued until he is able to eat, but usually smaller volumes are required. The value of plasma as a source of protein was proved experimentally in puppies, taking a protein-free diet, that flourished on plasma in contrast to litter mates that received amino acid hydrolysate intravenously or no protein.

Chief transfusion hazards are mismatching and typing errors, hepatitis (which can be controlled by storing plasma at room temperature six months or longer), citrate intoxication and bacterial contamination and potassium intoxication (which can be avoided by using blood within 10 days).

► [In these days when large quantities of blood and plasma are used it is important to realize that the danger of causing hepatitis has been practically eliminated by Dr. Allen's discovery that the simple device of stor-

**Use of Blood and Plasma in Surgical Practice.** According to J Garrott Allen and Edward A Stemmer<sup>7</sup> (Univ. of Chicago), blood transfusion is used principally for prevention and treatment of hypovolemic shock, correction of anemia when other measures will not serve equally well or better and in partial or complete exchange transfusions, as in erythroblastosis fetalis and monoxide poisoning Plasma is used in preference to blood in shock resulting from burns and peritonitis and in correction of hypoproteinemia in patients unable to eat Plasma is also useful as a standby or emergency fluid in treatment of hypovolemic shock until blood can be prepared Blood and plasma have specific advantages and risks, and proper choice between them and water and saline solutions is not always simple The following outline stressing the nature of the fluid disorder responsible for hypovolemia is useful, even though often more than one fluid has been lost.

Hypovolemic hypotension due to *blood loss* may be (1) external, as in lacerations or bleeding ulcer, or (2) internal, as in femoral fracture, crushing injury or ruptured spleen *Plasma loss* may be (1) external, as in burns, in which blood also may be lost, (2) internal, as in peritonitis, or (3) due to crushing injury, when generally more blood is lost than plasma In *water deprivation*, electrolytes are concentrated and not lost and indicated therapy is water without salt In *water loss*, as from vomiting, high intestinal pancreatic or biliary fistulas and diarrhea, generally electrolytes also are lost and water with electrolytes is needed

To estimate quantity of blood lost in surgical cases sponges and lap pads may be weighed A simpler method recommended by the authors is sponge and lap pad counts Approximate values for  $4 \times 8$  in sponges and  $6 \times 18$  in cotton lap pads are 10 cc and 100 cc, respectively Both weighing and counting of sponges have their greatest value in constantly reminding the surgeon that blood is being lost

Three guides are useful in evaluating type and volume of fluid a burned patient should receive (1) extent of surface area burned, (2) hourly urinary excretion and (3) patient's response to treatment If he remains in shock, more blood and plasma are indicated particularly if hemoconcentration is present If he becomes edematous, fluid and salt restric-

(7) S Clin North America 35 1597 1611 December 1955

tion may be necessary. Most patients whose burned surface area is under 15% require little or no parenteral fluid, but in elderly patients, some fluids should be given if burned area exceeds 10%. Total amount of fluid administered to burned patients during the first 24 hours is calculated by multiplying body weight in kilograms by percentage of skin area burned, times three. Thus, for a 70 kg man with a 35% burn, anticipated fluid requirement for first day is 7,350 cc, of which 3,675 (50%) should be colloid-bearing solutions, including blood, and 25%, or 1,840 cc, of 5% dextrose in water. Volume of fluids taken by mouth is deducted from calculated intravenous water requirement. If no fluid can be taken orally, 25% of the total is given as normal saline solution. The second day, volumes of all fluids are reduced by half. After the second day, parenteral fluids are seldom necessary, unless facial burns prevent eating and drinking. After 48 hours, salt intake is restricted to no more than 5 Gm/day, preferably less. Normal salt intake may be resumed at end of a week or 10 days.

In treatment of hypoproteinemia in patients who cannot take food by mouth, daily transfusion of a liter or more of plasma will elevate concentration of plasma proteins in three to six days. Smaller quantities are likely to have little effect in the depleted patient. Administration of 500 cc blood between transfusion of each liter of plasma corrects anemia and permits the patient to come to operation with normal concentration of both hemoglobin and plasma proteins. Postoperative administration of blood and/or plasma is continued until he is able to eat, but usually smaller volumes are required. The value of plasma as a source of protein was proved experimentally in puppies, taking a protein-free diet, that flourished on plasma in contrast to litter mates that received amino acid hydrolysate intravenously or no protein.

Chief transfusion hazards are mismatching and typing errors, hepatitis (which can be controlled by storing plasma at room temperature six months or longer), citrate intoxication and bacterial contamination and potassium intoxication (which can be avoided by using blood within 10 days).

► [In these days when large quantities of blood and plasma are used, it is important to realize that the danger of causing hepatitis has been practically eliminated by Dr. Allen's discovery that the simple device of stor-

ing the plasma at room temperature for six months gets rid of the infecting agent responsible for the disease—Ed ]

**Evaluation of Blood Transfusions by Determination of Total Hemoglobin in Surgical Patients** Olof Norlander<sup>8</sup> (Karolinska Hosp, Stockholm) determined the pre- and postoperative blood volume in 10 common abdominal operations and the variations in total hemoglobin postoperatively after the patients had received blood transfusions. The total hemoglobin was determined by Sjostrand's modified carbon monoxide method, which consists in determination of alveolar CO concentration before and after administration of small volumes of CO. The blood volume was computed from the value for total hemoglobin and for hemoglobin concentration in the blood. Blood losses were measured by weighing and measuring the blood in suction flasks. The amounts of blood administered during surgery were usually one to four times the blood losses.

Total hemoglobin values one to two days postoperatively were virtually unchanged by comparison with preoperative values. Blood volume and hemoglobin concentration showed considerably greater postoperative variation than did total hemoglobin values. No direct relation was demonstrable postoperatively between total hemoglobin and hemoglobin concentration. Reduction of hemoglobin concentration is an unreliable criterion for evaluating the magnitude of bleeding.

The study shows that there is considerable blood loss in the postoperative period, especially after prostatectomies, bladder resections and gastrointestinal operations. The *amount of blood replaced during and after surgery* should exceed the measured blood loss, without danger of overdosage. To insure the greatest possible reliability in blood transfusion therapy, the postoperative course should be checked with repeated blood volume determinations. The hemoglobin concentration is not as reliable an index as the blood volume. If the latter is not restored, there is danger of low protein levels in the body and of prolonged convalescence.

**Risk of Rapid and Large Citrated Blood Transfusions in Experimental Hemorrhagic Shock** Åke Senning<sup>9</sup> (Karolinska Inst, Stockholm) found that rapid transfusions of

(8) Acta chir scand nav 109 150 157 1955

(9) Ib d. 110 394-402 1956

heparinized blood in dogs with experimental hemorrhagic shock caused an immediate increase in blood pressure and minute volume. Similar transfusions with citrated blood usually caused a brief initial rise in blood pressure followed by hypocalcemic effects, i.e., a rapid fall in blood pressure, diminished minute volume and even cardiac arrest with a diminution of the power of the arterial blood to coagulate. The hypocalcemic effects are due to the ionized calcium in the receiver's blood becoming bound to excess citrate. If calcium ions are given intravenously, the citrate effect disappears. If cardiac arrest has occurred, cardiac massage is necessary to restart the circulation and get the calcium ions into the myocardium. The same effect can be brought about by massaging the heart long enough for the citrate to be metabolized and the calcium ions of the receiver to be mobilized from peripheral sources, after which the heart can continue to beat spontaneously.

It is recommended that calcium ions in the form of 10% calcium gluconate be given in connection with all rapid citrated blood transfusions.

► [There is no doubt that the intravenous administration of too much citrate can be harmful. Bruneau and the editor in 1943 demonstrated the fact clearly in dogs. The serious (even fatal) effect is not sufficiently appreciated. It is well, therefore, for Senning to re-emphasize the danger. —Ed.]

**Operative Risk in Patients with Coronary Heart Disease** was evaluated during the past five years in 5,778 surgical patients at the New England Center Hospital, Boston, by Benjamin Etsten and Samuel Proger.<sup>1</sup> Coronary heart disease was present in 517, 11 of whom had had myocardial infarction two days to seven weeks before surgery; 1,107 patients had no history of coronary heart disease but had unequivocally abnormal ECG's; 4,154 had no evidence of heart disease and normal ECG's. Age range was 40-90. Patients with no heart disease were predominantly under 60; those in the other two groups were mainly over 60. Total death rate for each group was corrected for age. In each group, about 60% of operations were major.

Of 15 postoperative deaths among the 517 patients, 6 were cardiac, 5 due to acute postoperative myocardial infarction and 1 to acute pulmonary edema. Two of 11 operated on of necessity shortly after myocardial infarction

(1) J.A.M.A. 159:845-848, Oct. 29, 1955.



died of myocardial infarction after surgery. The four postoperative cardiac deaths among 506 patients with chronic coronary disease, represented an incidence of 0.8%, about the same as that in patients with abnormal ECG's but no history of cardiac pain. Of seven deaths among the latter, four were due to myocardial infarction and three to acute pulmonary edema. Four postoperative, presumably cardiac, deaths in patients with no clinical or ECG evidence of heart disease were caused by acute pulmonary edema. Postoperative cardiac complications did not always prove fatal in patients with coronary heart disease, five survived postoperative myocardial infarction, and two recovered from acute pulmonary edema. Although the difference between 0.8% and 0.1% mortality rates in patients with coronary disease and those with no evidence of it, preoperatively, is statistically significant, the former figure is obviously low. Length of time of anesthesia and surgery apparently did not influence postoperative mortality rate, and there was no statistical difference in mortality rate related to anesthetic technic and agent.

The problem of surgery and anesthesia in the patient with coronary disease is inseparable from that of surgery in the elderly patient. Only when absolutely necessary should surgery be done within three months after evidence of onset of acute coronary heart disease with or without infarction.

It now appears that if a patient has survived an acute coronary heart episode and made the transition into the chronic stage, outlook for a long and productive life is good enough to warrant almost any operation that would otherwise be justifiable. Under such circumstances, risk of surgery is negligible as far as cardiac deaths are concerned. This should make patients with coronary heart disease much less reluctant to have recommended surgery and much less frightened when they do.

Experiences in Treatment of Surgical Patients Having Anuria and Uremia, related by W. J. Kolff<sup>2</sup> (Cleveland Clinic), with 17 case reports emphasize the cardinal principles of (1) maintenance of body fluid, (2) correct control of electrolytes, (3) suppression of protein breakdown (forced high caloric low protein diet) and (4) avoidance of

(2) Surg. Gynec. & Obst. 101:563-577, November 1955.

infection. If these measures seem to fail, or carry too great a risk, then elimination of retention products by use of the artificial kidney, peritoneal lavage or intestinal lavage is resorted to. Surgery or trauma may lead to renal failure directly or may provoke or coincide with accidents that cause it, such as coronary thrombosis, thrombosis of arteries to the legs, mesentery or kidneys, subarachnoidal hemorrhage, hepatorenal syndrome, pancreatitis, infusions of distilled water or mismatched transfusions. Often renal shut-down develops on the basis of pre-existing renal disease. The etiology may be impossible to ascertain in a given clinical situation, and, until proved otherwise, the patient must be treated in the hope that he has a curable disturbance of renal function.

**TREATMENT**—Attempts to prevent acute tubular necrosis include (1) restoration of low blood pressure with 6% dextran in 5% glucose (not in saline), which is better than blood unless blood is demonstrably lost. (2) In hemoglobinuric (incompatible blood) or myohemoglobinuric nephrosis (crush syndrome) the following may be of use if administered immediately: (a) 2,000 ml of 5% glucose plus 500 ml of 5%  $\text{NaHCO}_3$  intravenously (dangerous if given when kidneys are already blocked), (b) osmotic diuretic, 100 cc. of 25% mannitol intravenously (other diuretics are dangerous), (c) large exsanguinotransfusions to remove free hemoglobin. All other methods, including intermittent high spinal anesthesia, procaine intravenously and decapsulation seem to be either useless or harmful.

Once renal failure is established these measures are harmful. For further management it is important to recognize whether the patient is in an anuric (or severely oliguric) phase or a diuretic phase. Most patients with chronic uremia must excrete large amounts of urine, and for them treatment is as for chronic uremia. Some, however, are oliguric, notwithstanding sufficient hydration and should be treated as in acute anuria. For maintenance of body fluid in the anuric phase of acute anuria 700 ml/day plus compensation for loss is required, in the diuretic phase enough fluid to prevent dehydration. 2,000 or 3,000 ml/day, is necessary. If the patient is overhydrated during the anuric phase venesection is performed and sodium sulfate 5 Gm by mouth is given to cause diarrhea. The filtering type of artificial kidney is the most effective, or dialysis with dialyzing fluid made hypertonic by addition of glucose, either in the artificial kidney or in peritoneal lavage. In chronic uremia fluid often has to be forced sometimes with  $\text{NaCl}$ . Dialysis will correct hypotonic or hypertonic status of any electrolyte within a few hours, restoring all  $\text{Na}$  at one time should be avoided. In acute anuria, no  $\text{Na}$  should be given except to compensate for loss (this rule is modified in presence of acidosis). In chronic uremia, sodium lactate, 120 mEq/day is given to replace the  $\text{HCO}_3$  ion, with  $\text{NaCl}$  to replace

urinary loss. Rarely, a salt-free diet is given when indicated by hypertension, edema or cardiac failure. For hyperkalemia which is common in acute anuria, carboxylic resin sodium salt (30-60 Gm/day in divided doses, with care against overshooting, accompanied by a laxative), and hypertonic glucose (plus insulin) or invert sugar intravenously are used with a high-caloric low protein diet. If potassium excess is serious, dialysis is used. For hypokalemia, common in chronic uremia or in the diuretic phase of acute uremia, KCl is given slowly by vein (20 mEq in large volume diluent) or potassium gluconate by mouth. For hypocalcemia, 1 Gm calcium gluconate intravenously and aluminum hydroxide, to bind potassium in multiple doses to tolerance (5-10 ml 12 times daily) are administered.

For acidosis in acute anuria or uremia, carbohydrate is given and rarely, sodium lactate (40 mEq) or sodium bicarbonate (4 Gm daily), only if  $\text{HCO}_3^-$  ion is lower than 12 mEq/L. Dialysis is used to remove abnormal acids. For acidosis of chronic uremia, sodium lactate, 120-180 mEq/day is used, and K gluconate if potassium ion is also low. Dialysis is rarely used.

Protein catabolism is suppressed with a high caloric, low protein diet. Transfusions and surgery are avoided, if possible, because they increase protein catabolism. Forced high caloric (over 2,000 cal), low protein (20-40 Gm) diet is useful in chronic uremia, in acute uremia, administer as much as practicable, keeping careful record of caloric intake. Fat emulsion can be tried by mouth or (diluted) by gastric drip. If necessary, 20% invert sugar plus insulin intravenously or hypertonic (to 40%) glucose or invert sugar may be given by cardiac catheter. Intravenous fat emulsion may be practicable in the future.

In prophylaxis and treatment of infections, erythromycin seems well tolerated. Streptomycin, when not excreted, may accumulate and cause irreparable vestibular (nerve) damage. For elimination of retention products by dialysis, five or six hours with the artificial kidney will suffice and its effect will last four to seven days. Peritoneal lavage is not often possible in postoperative patients, and electrolyte regulation is difficult with intestinal lavage.

► [This is an excellent presentation of the whole subject with also a discussion of the use of the artificial kidney, one of the modern therapeutic miracles. Anyone interested is urged to read the whole article—Ed.]

**Interpretation of Biochemical Effects of Injury and Ischemia** Ian W. MacPhee and Dorothy Turnock<sup>3</sup> (Univ of Liverpool) state that retention after operation or injury of sodium, chloride and water is well known and that fluids and electrolytes should not be administered unless deficiency is shown. The absence of sodium chloride from the urine in the first postoperative week is not evidence of salt deficiency.

Experiments with rats that have had one hind leg tied

with a tourniquet for two to four hours, to obliterate the arterial circulation, show depletion of potassium and increase of sodium and water in the muscle cells. This also happens in the tourniquet limb in adrenalectomized rats. Potassium content of interstitial fluid increases and there is an increase in the interstitial water, in the form of edema. Application of the tourniquet for four hours leads to cell necrosis, whereas effects from tourniquet application for only two hours are reversible. Cell death possibly can be detected by electrolyte changes before morphologic evidence of cell destruction can be seen.

In intact animals some loss of cell potassium and increase in cell sodium is detected in the contralateral undamaged leg, but the changes are not so marked as in the ischemic limb. In adrenalectomized animals, no such changes occur. The changes in the undamaged muscle seem due to or governed by adrenocortical activity.

An anoxic state causes transudation of potassium from the cell to the extracellular phase. If the peripheral circulation failure is such that renal function is impaired, and excretion is negligible, the potassium may cause toxic symptoms. Increased potassium concentration in the blood is a reflection of the severity of tissue anoxia and tissue damage and is not evidence of impending death.

The return of sodium and water from the cells is slower than from extracellular space. The continued leakage of water, protein and electrolyte into the damaged tissue spaces may be made more serious by the passage of water and electrolyte into damaged cells, where they are not only lost but temporarily beyond recall. Loss of fluid and electrolyte not only into the tissue spaces but also into the cells, both damaged and undamaged, may account for some of the features of irreversible shock.

**Increased Excretion of Aldosterone Immediately after Operation.** By bioassay, J. G. Llaurodo<sup>4</sup> (Univ. of Otago, Dunedin, New Zealand) detected aldosterone in the urine of six patients both pre- and postoperatively. Some patients excreted aldosterone preoperatively, but all excreted it in much larger quantities postoperatively. Aldosterone, an electrolyte-regulating corticoadrenal hormone, causes the retention of sodium and the excretion of potassium. The

(4) Lancet 1 1295 1298 June 25 1955

positive sodium and the negative potassium balance seen after surgical trauma is due to aldosterone activity. The increased excretion of the aldosterone was accompanied by a sharp potassium loss and sodium retention. Excretion levels of the corticoid correlated qualitatively with the  $\text{Na}^+/\text{K}^+$  ratio in the urine of patients before and after operation.

The bioassays were made with pure crystalline aldosterone. This steroid is 100 times as strong as desoxycortone when assayed in terms of  $\text{Na}^+/\text{K}^+$  urinary deviation in the rat.

► [This interesting finding is of great importance to our proper understanding of postoperative and post-traumatic electrolyte metabolism.—Ed.]

**General Hypothermia in Treatment of Massive Hemorrhages. Study of Possible Additional Applications in Transfusions of Blood and Blood Substitutes.** P. Goffrini and E. Bezzi<sup>5</sup> (Univ. of Parma) cite previous investigations by themselves and others on experimental shock demonstrating that pharmacologic sympathetic block and refrigeration guarantee a higher survival rate than is found in untreated control animals. Larger quantities of blood can be withdrawn without causing death, and limits of recuperation time following replacement of blood are extended. Thus artificial hypothermia has a protective effect in shock syndromes by inhibiting harmful vasomotor reflexes and reducing oxygen need.

In the present study arterial pressure, ECG and respiration were determined in animals in extreme hypoxia while circulating blood volume was maintained by replacement with macromolecular solutions. The results appear to establish a difference between the roles of acute hemodynamic imbalance and of anoxia in death from massive acute hemorrhage. In a first stage changes caused by bleeding and emptying of the cardiac cavity and large vessels can be reduced by vascular replenishment with solutions not carrying oxygen. Conversely in a second stage accompanying progressive diminution in hemoglobin and hematocrit disturbances of conduction appear which can be attributed solely to effects of anoxia. Controlled hypothermia proved efficacious in increasing the general resistance of the organism and particularly of the heart disordered by massive

(5) *Presse med.* 63:847-851, June 1, 1955.

hemorrhage or prolonged and serious hypoxia. Possible practical applications in treatment of acute hemorrhagic states are outlined.

To avoid death by exsanguination, it is urgently imperative to restore circulating blood volume, when suitable blood is not available, with any liquid that does not escape too rapidly from the vascular system. When blood volume is restored by a blood substitute, however, danger from anemic anoxia remains. Slowing of oxidative processes by refrigeration permits survival of animals for a remarkable time under conditions of hematosia absolutely incompatible with normal life, thus allowing opportunity for beneficial and decisive intervention. This treatment also would be advantageous in clinical cases of acute hemorrhage, which are but rarely of comparable gravity. Although transfusion of whole blood is the procedure of choice in acute hemorrhagic states, with controlled hypothermia, the value of blood substitutes is enhanced. This may be important in situations of extreme emergency when blood supply is unavailable or insufficient. Tolerance to exsanguination in animals with induced hypothermia suggested that quantitative and qualitative replacement of lost blood might be modified. Hemorrhagic states requiring modified replacement are those in which it would seem desirable to maintain arterial hypotension for some hours, to cause spontaneous hemostasis, when surgical hemostasis is impossible. Hypotension should not exceed in degree or duration the limits imposed by risk of cerebral or renal lesions.

Man, 58, had multiple massive hemorrhages four days after an extensive operation, involving multiple anastomoses, for postanastomotic ulcer after previous gastrectomy. During the first four hours, repeated transfusions (8 L. whole blood plus 3.5 L. macromolecular fluid) were given; but as soon as arterial pressure mounted toward 100 mm. Hg, another hemorrhage ensued. When blood pressure remained around 70, hemorrhage ceased. Rectal temperature was then reduced to 30 C. in 2½ hours and arterial pressure was maintained at 65/70. Shivering and restlessness did not appear until four hours after induction of refrigeration. Transfusion of 300 ml. whole blood given slowly increased blood pressure to 80 without provoking a new hemorrhage. After 12 hours of hypothermia, pressure was 90/50. Rectal temperature varied from 30 to 33 C. He was rehydrated with physiologic salt solution with ganglioplegics and procaine added. Active refrigeration was terminated after 14 hours, and temperature returned slowly to normal within 8 hours. Therapeutic

transfusion (whole blood and plasma) was delayed until 28 hours after onset of hemorrhages, and pressure returned to 125/75 at end of the second day. He recovered completely and left the hospital the 14th day.

Undoubtedly, continuing classic treatment would have had uncertain results, since vital processes were being adversely affected by successive episodes of hypotension, along with generalized shock, caused by exhaustion and endocrine metabolic reserves.

Prolonged tolerance of massive blood loss suggests using alternate withdrawal and substitution of blood in larger quantities, which would simplify technic and reduce dangers inherent in successive disturbances to circulatory equilibrium in exsanguinating transfusions.

► [This interesting idea has many potential applications in cases of severe hemorrhage, and it should have a place in military surgery.—Ed.]

**Experimental Evaluation of Prolonged Hypothermia**  
Bernard Fisher, Clam Russ, Edward Fedor, Ralph Wilde, Perry Engstrom, John Happel and Paul Prendergast<sup>6</sup>

(Univ. of Pittsburgh) report observations on 20 dogs maintained for 6.5-31.5 hours at a mean temperature of  $23.5 \pm 0.7^\circ\text{C}$ , with ether as the anesthetic agent to control shivering. Body temperature could be maintained by adjusting ambient temperature. Each dog had its own critical temperature, usually between  $22.5$  and  $24.5^\circ\text{C}$ , at which point no further ether was needed to control shivering. No need was found for positive-pressure respiration down to temperatures of  $21^\circ\text{C}$ , and during prolonged hypothermia animals maintained respiratory minute volumes.

During temperature stability (2-24 hours), pulse rate continued to decline gradually, the mean rate for the first 8 hours being 61, for the second 8 hours 54 and for 16-24 hours 48. Minor increases in temperature were accompanied by significant increases in pulse rate. The ECG's showed some prolongation of the QRS complex and lengthening of the QT interval, but no regular specific change of prognostic importance was noted. In 15 animals, increase of hematocrit values was  $35 \pm 18\%$ , only 3 showing a change of less than  $15\%$ . One animal had a hematocrit value of 92 after 17 hours of hypothermia. Venous pressure decreased in 10 of 14 animals, and in the other 4, elevation was slight. By the end of the first hour of cooling, arterial blood pres-

(6) A M A Arch Surg 71 431 448 September 1955

sure decreased an average of 23% and then progressively declined. At 8, 16 and 24 hours, mean values were 33, 44 and 67% less than before cooling.

Alterations in clotting are present early in hypothermia, and by the fourth hour all animals demonstrated significant increase in coagulation time and at six hours, in prothrombin time. In all dogs, at some point during hypothermia blood would not clot and it was impossible to determine prothrombin. After 4 hours, coagulation time was over 70 minutes in one dog, and the earliest complete breakdown in prothrombin time was at 14 hours. Every animal showed decrease in plasma specific gravity and in plasma protein levels, the average decrease of the latter being  $33 \pm 15\%$ . Average blood sugar level before anesthesia was 72 mg/100 cc, and after about one hour of ether, 127 mg. Mean terminal blood sugar level was 46 mg, a decrease of  $63 \pm 18\%$  for an average of 19 hours of hypothermia.

Changes in serum sodium, calcium and potassium levels were not statistically significant. Chloride levels increased 7% in the nine animals observed. Precooling chloride levels were  $110 \pm 6$  mEq/L, and mean final readings were  $118 \pm 5$  mEq/L. Serum phosphorus level in seven animals was  $282 \pm 0.61$  mEq/L before and  $360 \pm 1.44$  mEq/L after cooling, a 28% increase. Most animals showed significant drop in pH during early hours of hypothermia, with decrease in  $\text{CO}_2$ . Slight increase in  $\text{pCO}_2$  occurred, indicating that acidosis, although predominantly metabolic, had some respiratory component. By maintenance of a large minute volume of respired air,  $\text{pCO}_2$  was kept below or at normal. This was in the presence of a low pH and a decreased  $\text{CO}_2$ , indicating that acidosis was metabolic in type during prolonged hypothermia. Ability to compensate for changes in acid-base balance was not lost even after many hours of cooling.

Under conditions of these experiments there appeared to be no relation between ventricular fibrillation and blood pH, plasma  $\text{CO}_2$ , potassium level, venous pressure, hematocrit value, etc. Drop of blood pressure below 40 mm Hg was almost prognostic of death within a short time. Animals could not be kept alive with any regularity below 22 C early in hypothermia or after many hours, despite results unchanged from those at 23 C, at which survival was greater.



Prolonged hypothermia at 22-24 C, where oxygen consumption is 15-20% of normal, is not akin to hibernation or relative physiologic inactivity, for, though temperature may remain stable, progressive changes occur with length of hypothermia. Many enzyme systems apparently are interfered with as hypothermia is prolonged, and it remains to be proved whether such changes are only temporary. Though hypothermia has been used with relative safety in some patients, it still must be considered experimental. Results of the study suggest that the longer hypothermia exists, the more complex and pronounced the changes from normal and possibly the more difficult to correct.

► [More studies like this are desirable in order to increase our knowledge of this interesting and important new technic—Ed.]

**Comparison of Blood Loss and Operative Time in Certain Surgical Procedures Completed with and without Controlled Hypotension** was made by John W. Ditzler and James E. Eckenhoff<sup>7</sup> (Univ. of Pennsylvania). Controlled hypotension was used in 90 patients, and similar operations were performed on 84 without controlled hypotension. To produce hypotension, arfonad<sup>®</sup> was used in 65 patients, spinal anesthesia in 19, hexamethonium in 4 and protovera trine A and B in 2. Blood loss was measured by the "dry sponge" gravimetric method. To the figure obtained was added the amount of blood collected in the suction bottle.

Blood loss averaged 910 ml. in 29 patients who had radical dissections of the neck during deliberate hypotension, and 1,415 ml. in 20 control patients. Average operative time was 4 hours 45 minutes with controlled hypotension and 3 hours 50 minutes without. In 17 patients who had radical dissection in the pelvis with induced hypotension blood loss averaged 1,870 ml., and in 11 controls 2,805 ml. Average operative time was 5 hours with deliberate hypotension and 4 hours 35 minutes in the controls.

The study shows that hypotensive anesthetic techniques reduce the amount of blood lost during major operative dissection. It is difficult to determine whether such reduction is sufficient to justify the hazard involved. There was no reduction in operative time. Deliberate hypotension is not used without considerable risk to the patient. One patient died from sudden cardiac arrest and two from uremia.

subsequent to prolonged abdominal operations. The production of deliberate hypotension is a formidable procedure. It should be undertaken only by those trained in the use of the technique and those fully cognizant of the physiology of hypotension, the pharmacology of the drugs used, the adjuncts assisting to induce hypotension and the limits of the method. Only 100 mg arfonad<sup>2</sup> should be used in the first 15 minutes of operation and only 1 Gm for the entire operation. The ganglion-blocking agents reduce the need for general anesthesia and reduce pulmonary ventilation, which must be corrected by adequate tidal exchange.

**Nitrogen Metabolism in the Surgical Patient.** William D Holden<sup>8</sup> (Western Reserve Univ.) states that the metabolic disturbances which occur in most surgical patients are mild and temporary and that convalescence is usually progressive and rapid. However, when nutritional and electrolyte disturbances exist before operation, when the magnitude of operative trauma is great and when convalescence is impeded by a series of complications, considerate attention to the disturbed metabolic processes can mean the difference between death and ultimate recovery of the patient. The homeostatic capacities of the body are usually adequate to restore the normal metabolic balances.

Nitrogen metabolism is a small but vital part of all metabolic activity. The proteins and amino acids of the body are in a constant state of dynamic equilibrium. Anabolic and catabolic reactions go on constantly and simultaneously. Surgical trauma produces alterations in nitrogen metabolism, but there is considerable variation from patient to patient. The pattern of nitrogen response to trauma is influenced or modified by many factors, among which are age, sex, part of the body traumatized, renal function, electrolyte balance, fluid administration, complications of surgery, hormonal changes and the energy requirements of the body.

The normal adult has a catabolic response to surgical trauma. It breaks down proteins and has an increased nitrogen excretion. The extent and rate of destruction of tissue protein as well as the inability of the body to utilize administered amino acids for protein synthesis, parallel the severity of the trauma. Patients do not recover from the effects of an operation unless the catabolic process diminishes and th

(8) Am Surgeon 21 434-441 May 1955

body accepts nitrogen for restoration of lost protein. It is not known if postoperative nitrogen wastage is beneficial or injurious. The protein that is broken down is used largely for energy purposes, and it is very likely that immediate postoperative energy requirements initiate hydrolysis of body protein.

When a patient who has been deprived chronically of protein is subjected to a major surgical procedure, there is no more than a slight transient increase in quantity of nitrogen excreted. Intensity of the biologic response is reduced markedly. The patient who undergoes two major surgical procedures within a short time frequently manifests a much less intense catabolic response to the second operation. The diminished secondary catabolic response to surgery occurs in the presence of either acute or chronic protein depletion. The quantity of nitrogen lost from the body during the postoperative period can be reduced by providing the patient with a large number of calories in the form of nutrients that are oxidized readily for energy purposes. However, exact energy requirements of the postoperative patient are not known.

► [Studies such as this demonstrate clearly the fact that no operation is as innocuous as is sometimes believed.—Ed.]

**Surgery and Rehabilitation.** O. Bistrom<sup>9</sup> (Univ. of Helsinki) states that, since rehabilitation is an integral part of surgery, every surgeon must assume the responsibility not only for treating the pathologic disorder but also for reconditioning a disabled individual physically and mentally and thus equipping him for a productive life. In a wide sense rehabilitation includes all the measures required to restore the patient's ability to earn his own livelihood. In addition to medical, surgical or psychiatric treatment, physical therapy, occupational therapy, psychophysiologic tests, vocational guidance and training and employment service are necessary. The surgical therapy should be designed not to cause undue impairment of any part of the body, especially the extremities. The patient should be kept as mobile as his condition permits. In pathologic states of the extremities, the muscular activity and mobility of uninvolved joints should not be impaired.

The will of the patient to get better and return to work is

(9) *Ann. chir. et gynæc. Fenniae* 44:27-35, 1955.

very important. The aid of psychologists, educational officers and social workers is often needed.

A case is presented of a man, 44, with spinal tuberculosis who had been bedridden for 21 years. Immobilization was considered necessary, but rehabilitation of the patient was ignored. The combined efforts of the surgeon and social, educational and vocational workers allowed the patient to get out of bed and to begin to walk with crutches and earn his living.

**Injurious Effect of Cortisone on Destructive Inflammation.** O. Bistrom<sup>1</sup> (Helsinki) reports on seven patients with destructive, nonspecific or tuberculous inflammations of the bone, first treated for many months with cortisone or hydrocortisone under the erroneous diagnosis of rheumatic polyarthritis or deforming arthrosis. Both general and local symptoms of the inflammation were more or less alleviated during the treatment. Immediately after termination of cortisone therapy, the bone lesions were aggravated, and destructive changes became severe. In some patients, abscesses formed. Despite severe destructive changes, the patients responded favorably to specific antibiotics and chemotherapy. The uncritical use of cortisone leads to aggravation of certain inflammatory conditions.

Woman, 38, never had had tuberculous manifestations but occasionally had severe rheumatic pain in various joints. Chronic polyarthritis was diagnosed, and she received cortisone for two months. Recovery was rapid, but soon after discharge and termination of treatment, an abscess developed in the region of the right hip. The abscess was opened, and a permanent fistula resulted. A bony defect 3 × 4 cm was found in the right iliac bone. At operation, a passage between the fistula and the defect was found. The defect was filled with cheesy necrosis. Tubercle bacilli were cultured. Postoperatively, the fistula closed during specific treatment.

► [This phenomenon is now rather well known in this country.—Ed.]

**Newer Experimental Results in Tissue Transplantation** are reported by G. Ruhenstroth<sup>2</sup> from the Max-Planck Inst for Biochemistry, Tübingen. Research on tissue transplantation has made great progress in recent years even though only isolated practical inferences can be drawn. Results indicate that future developments may be significant in experimental and clinical medicine. As a rule, transplanted tissue undergoes necrosis, with inflammation in the tissue

(1) Acta chir. scandinav. 109:200-202, 1955.

(2) Deutsche med. Wchnschr. 81:474-475, Mar. 30, 1956.



munologic paralysis." Pretreatment must be specific in that cells first injected must be genetically related to later experimental cells, but freeze drying does not destroy their effect.

These observations show that there are two ways to promote grafting of larger and thicker heterotransplants—by general reduction of antibody formation and by active acquired tolerance against certain foreign tissues. Future developments will show whether either of these will be significant in clinical medicine.

**Tissue Reaction to Implanted Plastics** was studied in rats and rabbits by Jens Bing<sup>3</sup> (Copenhagen). Implantation of polyethylene film, in the form of small balls with a smooth surface in some animals and of fine pieces of the same thin film in others, resulted in considerably different tissue reactions. Reaction to the smooth parts of the balls consisted in a capsule of connective tissue lined with a single layer of vascular endothelium. Reaction to small pieces of film was more pronounced with many foreign body giant cells. Polyethylene mesh woven of threads of the plastic produces a tissue reaction similar to that observed in experiments with Nylon suture material. Polyethylene mesh made from shavings from blocks of the plastic produced the same slight tissue reaction caused by implantation of polyethylene "Polystan sponge," which is made of similar material.

The plastic sponge "Ivalon," derived from formalinized polyvinyl alcohol, has been thought to be nonabsorbable and is being advocated for permanent prostheses. After subcutaneous and intraperitoneal implantation into rats, fibrin threads and leukocytes were evident on the 3d and 5th days. A week after implantation, connective tissue was seen growing into the meshes from surrounding subcutaneous tissue and from omentum, with a few foreign body giant cells. In sponges removed over a month after implantation, connective tissue reached the center of the piece, collagen fibers forming thicker bundles in subcutaneous than in intraperitoneal implants. Connective tissue contained giant cells and some mononuclear macrophages with large cytoplasm containing droplets. The sponge was undoubtedly partly resorbed, since some pieces decreased in size, although meshes in the sponge were widening. Resorption of

(3) *Acta path et microbiol scand nav* suppl 103 pp 16-26 1955

Ivalon sponge was still more evident after subcutaneous implantation in three rabbits. Definite decrease in size and change of texture had occurred after 7 months, and after 1½ years no sponge was visible grossly or microscopically after biopsy. When "Ivalon" was compressed to a film before implantation, tissue reaction was less pronounced and giant cells were seen only where rests of spongy structure were retained.

These experiments with polyethylene and Ivalon sponge demonstrated that tissue reaction is determined largely by physical rather than chemical characteristics of the plastic. ► [The effort on the part of the tissues to expel a foreign body still goes on. Will the reaction ever be otherwise?—Ed.]

**Reaction of Serous Cavities to Blood**, according to John S. Chapman<sup>4</sup> (Univ. of Texas), has never been fully studied. From clinical reports it is evident that uncontaminated intraperitoneal bleeding gives rise to peritoneal pain, leukocytosis and, in some instances, shock. In one study, several patients who received intraperitoneal injections of their own blood had mild leukocytosis (12,000) and slight temperature elevation (100 F) within two to six hours. That such a reaction is not peculiar to the peritoneum is suggested by experience in injuries of the pleura which result in aseptic hemothorax, with mild fever and leukocytosis. Studies of aspirated fluid revealed a cellular distribution different from that of circulating blood, and relative proportion of cells varies with time elapsed following injury. Another group of patients has been reported in whom unusually high eosinophil counts were found in pleural fluid present 10 days or more after various types of pleural injury, which must have resulted from the patients' own blood.

Experiments to elucidate these clinical findings by injection of blood into the peritoneum of mice produced a cellular reaction characterized both locally and systemically by early polymorphonuclear leukocytosis, later lymphocytosis and still later a rather persistent eosinophilia. Changes in peripheral blood seemed to precede those in peritoneal smears by about 24 hours. A special characteristic of the peritoneal cellular reaction was appearance of large mononuclear phagocytes containing an iron-bearing pigment. Re

action was the same regardless of whether blood was clotted, unclotted, heparinized or citrated

The reaction cannot be one of hypersensitivity, since autogenous blood evokes it and since the reaction to heterogenous blood is seemingly independent of antibody formation

These observations may explain why patients with effusions of blood into their peritoneum or pleura often present polymorphonuclear leukocytosis and why the fluid drawn from these cavities may show mild cellular reaction and occasionally marked eosinophilia. In such cases, if microscopy does not reveal red cells, a benzidine test may be of interest. Possibly, but not certainly, serous membrane reaction to blood may explain the fluids sometimes seen clinically which seem to fall in a vague zone between exudates and transudates. Further studies are in process to determine what portion or portions of blood produce these serous reactions.

**Capillary Hemangiomas of Skin** John J. Modlin<sup>5</sup> (Columbia, Mo.) reports on 42 children (29 girls) with 52 capillary hemangiomas (4 with a partial cavernous component) observed since 1947. Although 44 hemangiomas were noted within a week after birth, and 48 had a history of rapid growth, only two children were examined before two months. Except for one boy, 6, all others were seen before age 2. Twenty-five lesions involved face, neck or scalp, 17, extremities and 10, the trunk. Eleven were surgically excised, 10 received "token" irradiation (250 or 500 r) to placate anxious parents and to prevent more vigorous treatment elsewhere, and 31 were not treated. Complete regression occurred in 24 (61%) of 39 untreated lesions, and regression is continuing in all but one of the remaining 15. In no case was there progression of a hemangioma after 1 year of age, nor was there destruction of features, serious hemorrhage, malignant degeneration or loss of life. Ulceration occurred in six hemangiomas, with spontaneous healing in five (one was lost to follow-up). Bleeding occurred in three of the six ulcerated lesions but was not serious. Disappearance of hemangiomas appeared to be hastened in lesions which ulcerated. After the lesions regressed completely the site of former hemangioma could be detected



as a white, slightly scarred area in 15 and as a raised projection (without red discoloration) in 3; in 6, the site was difficult to detect. Length of time necessary for complete regression varied from one to four years. Some children, however, will be over 5 at time of complete regression, e.g., in one girl, 5½, two hemangiomas are still undergoing regression (Figs. 4 and 5).

The ideal treatment of infantile capillary hemangiomas consists of destruction or surgical excision early in life before the characteristic rapid growth occurs. The fact re-



Fig 4



Fig 5

(Courtesy of Modlin, J J Surgery 38 169 180, July, 1955)

mains, however, that many lesions will be seen after enlargement has occurred, and it appears that these may be followed closely without treatment. Frequent examinations, with careful measurements and color photographs, provide a tangible means of reassurance of apprehensive parents. Judicious restraint may produce a much better end result than that following well meant but vigorously applied destructive treatment. There is need for additional reports of conservatively managed cases to determine the true natural history of these lesions.

► (This careful study with its evidence of frequent regression is a powerful argument for the conservative treatment of these lesions so distressing to the parents —Ed)

Surgical Aspects of Coccidioidomycosis are reported by Howard D Cogswell<sup>6</sup> (Tucson, Ariz.) Human coccidioidomycosis, due to infection by the fungus *Coccidioides immitis*, is endemic in certain areas in southwestern United States, northern Mexico, Argentina and Uruguay. Most patients have visited the areas previous to onset of the disease, which is usually acquired by inhaling fungi-laden dust. The fungi may be carried by the blood or lymphatics to distant organs, disseminating the disease. The first phase of the disease, or primary infection, is usually limited to the lung area. In the second phase, disseminated infection, numerous portions of the body may be affected by the coccidioidal granulomatous lesions, which may prove fatal.

The coccidioidin skin test is a useful diagnostic aid, the complement fixation test is of value in the later and more serious infections. Microscopic and culture studies furnish the most indisputable proof of the disease. In lesions accessible for biopsy, the microscopic picture is definite and diagnosis can be made without doubt. There is no specific form of therapy, and the known chemotherapeutic agents or antibiotic drugs have been ineffective.

Surgery can be used for some of the localized lesions, such as those in the skin, perinephric area, kidneys, lungs, bones, cervical lymph glands and pelvic adnexa. The lesion may be excised, or drained when excision is not possible. Surgery cannot be used during the disseminating stage.

The chest lesions are the most common foci of the disease needing surgery, which is indicated by (1) large, blocked or expanding cavity, (2) spontaneous pneumothorax with a nonexpansible lung, (3) hemoptysis with a persistent cavity and (4) tumor, in older patients, that cannot be definitely diagnosed as coccidioidomycosis. Segmental resection and lobectomy are the common operations. The incidence of bronchopleural fistula after surgery is probably higher than is known, other complications are recavitation and empyema. Mortality and morbidity rates are low.

Infections in extrapulmonary viscera are common in the disseminated form and are rare, and represent residual infection, after the disseminated coccidioidomycosis has become stabilized. Bone lesions are the most common complications. Some lesions require amputation because of osseous

fistulas, pain, deformity and disability. Immobilization, rest and occasional incision and drainage constitute the treatment of choice in coccidioidomycotic bone lesions until a specific chemotherapeutic agent is discovered.

The lesions frequently become secondarily infected with the ordinary pathogens after spontaneous rupture or incision and drainage of the abscesses. Antibiotics are of great value in controlling the mixed infection, often more severe than the original infection.

**Demonstration of Toxic Factor(s) in Thermal Death**  
Alfred B. Chaet<sup>7</sup> (Univ. of Maine) found that immersion of the posterior half of the marine worm, *Phascolosoma gouldii*, into hot sea water ( $76 \pm 1^\circ \text{C}$ ) for 90 seconds caused death of the worms in about 21 hours. When a ligature was tied around the middle of the worms before immersion, thus preventing the celomic fluid in the scalded portion from mixing with that in the anterior portion, survival time was increased. When the celomic fluid was removed from worms 15 minutes after scalding and injected cephalad into the posterior end of normal recipient worms, the worms died. When celomic fluid from normal worms was injected into other normal worms, death did not occur. It appears then, that scalding releases a toxic substance which is found in the celomic fluid. Further experiments showed that toxin was not released in scalded animals in which sea water was injected into the celomic cavity to replace celomic fluid. This suggests that the toxic substance originates in the celomic fluid. Other experiments demonstrated that the toxic factor can be released merely by heating celomic fluid *in vitro* since animals receiving injections of this fluid died in about 40 hours. It appears that the toxin can be released without any interaction between celomic fluid and the rest of the organism. The toxic factor was found to be released only in that fraction of the celomic fluid containing the cells.

The toxic factor was still active after autoclaving. It was not ether soluble and its toxicity was not due to any pH change or potassium content. The factor was partially isolated by saturation with ammonium sulfate.

► [This is an interesting idea that should be further developed. Yet it does not seem surprising that tissues altered by scalding (or burning) should yield toxic substances.—Ed.]

## TECHNICAL CONTRIBUTIONS

**Induction and Control of Hypothermia.** M. H. Cass (Melbourne) A. F. A. Harper and R. G. Wylie<sup>8</sup> (Sydney) list the necessary qualifications of a good hypothermia technic. (1) It should be possible to lower, maintain and subsequently raise the subject's temperature in a controlled manner. (2) Equipment should be simple and convenient to operate. (3) There should be as little interference as possible with normal anesthetic management, antiseptic precautions and surgical access. (4) Dangers arising from the technic itself should be kept to a minimum, such as risk of frost-bite or burning, and the subject should be accessible for immediate remedial measures should fibrillation or cardiac arrest occur. (5) The over-all time for induction of the desired degree of hypothermia and the subsequent rewarming should be as short as is practicable.

The various technics used are shown in Table 1 and the characteristics of these in Table 2. The best method employs a set of rubber blankets through channels in which water is circulated, supplemented during the cooling stage by use of ice bags. The method is easy to apply, rate of change of temperature is as rapid as seems safe, there is full control of the subject's temperature at all stages, cooling can continue in the preparatory stages of operation, warming can commence in its concluding stages, surgical access in an emergency is easy and there is no interference with asepsis.

Five blankets are used, two for the thighs and one each for the lower trunk, thorax and back. In each blanket the water flows through a continuous channel of  $\frac{1}{2} \times \frac{1}{4}$  in. cross-section formed by the gaps between rubber septa projecting alternately from either end of the blanket to near the other end, and bounded top and bottom by rubber sheets. Rubber tubing connects the blankets to a manifold, into which water is pumped from a tank containing ice and water. Water at about 40 C. is used to rewarm the subjects. Cooling is assisted by ice bags. Experiments on sheep with the blankets and ice bags reduced the temperature (normal for sheep, 38 C.) to 28 C., with a cooling rate of 4.8 C./hour

TABLE 1—TECHNIQUES FOR HYPOTHERMIA, WITH OBSERVED RATES OF CHANGE OF TEMPERATURE

TECHNIC FOR HEATING OR COOLING	REFERENCE	RATE OF CHANGE OF TEMP (DEGREES C/Hr) AND TEMP OVERSHOOT (DEGREES C, IN ITALICS)				
		Dog	Monkey	Sheep	Child	Man
Lytic cocktail' of pethidine, prometha- zine and chlorprom- azine	Laborit as quoted by Dundee, Gray <i>et al</i> (1953)					-0
	Smith and Fairer (1953)					0
	Shackman <i>et al</i> (1954)					-4
	Ripstein <i>et al</i> (1954)	-30				-3, 1 +4
	Delorme (1952)	-12 +18 to +24 -11, 2 to 3			-6 to -33, 2 to 8	-6 to -8, 7
Circulation of blood in external coil Circulation of saline in pleural cavity Bath, iced water	Blades and Pierpont (1954)					
	Churchill Davidson (1953)					
	Swan <i>et al</i> (1953)		-10 to -30, 2			
	Callaghan <i>et al</i> (1954) Edwards <i>et al</i> (1954) Lynn <i>et al</i> (1954)	-3 to -4				
	Swan and Zeavin (1954) This paper			-13, 2		
Bath, warm water	Bigelow, Lindsay, Harrison <i>et al</i> (1950)	+8				
	Callaghan <i>et al</i> (1954)	+9 to +25				
	Fleming (1954)	+9				
	Lewis <i>et al</i> (1954)					
	Smith and Fay (1940)					
Ice packs Ice packs with chlor- promazine	Dundee, Gray <i>et al</i> (1953)				+10 to +17	+6 to +10
	Dundee, Scott and Mesham (1953)	-7				-2, 2
	Bigelow <i>et al</i> (1954)					

TABLE 1 (Cont)

TECHNIC FOR HEATING OR COOLING	REFERENCE	RATE OF CHANGE OF TEMP. (DEGREES C/Hr.) AND TEMP. OVERSHOOT (DEGREES C, IN ITALICS)				
		Dog	Monkey	Sheep	Child	Man
Cold or warm air	Bigelow, Lindsay and Greenwood (1950)	-6 -3 to -1 +4				
	Bigelow, Lindsay, Harrison <i>et al</i> (1950)					
Electric blanket heating	Cookson, <i>et al</i> (1952)					
	Cookson, <i>et al</i> . (1952)					
Radiofrequency heating	Bigelow, Callaghan and Hopps (1950)	+3 to +13				
	Bigelow <i>et al</i> (1954)					
Large "blankets" for circulation of liquid	Callaghan <i>et al</i> (1954)		+9 to +25			
	Bigelow, Callaghan and Hopps (1950)					
As above, with chlorpromazine	Bigelow and McBurnie (1953)	-1	-18 to -36		-10 -1 to -5, 3	-2 to -1, 3
	Tleming (1954)					
Set of "blankets" for circulation of liquid with chlorpromazine	Inglis <i>et al</i> (1954)			-3, 0.3 to 1 +3		-1 -2 +2 -1, 0.7 +3
	Lewis <i>et al</i> . (1954)					
	Pontius <i>et al</i> (1954)					
	Ripstein <i>et al</i> (1954)					
	Bigelow <i>et al</i> (1954)					
	Ripstein <i>et al</i> . (1954)					
	This paper					

TABLE 2—CHARACTERISTICS OF TECHNIQUES FOR HYPOTHERMIA

METHOD OF COOLING OR REWARMING	CONTROL OF RATE OF CHANGE OF TEMP			EASE OF APPLICATION	ANESTHETIC MANAGEMENT	ASEPSIS	SURGICAL ACCESS	
	During Cooling	During Operation	During Rewarming				During Cooling	During Operation
Lytic cocktail'	Poor	Poor	Poor	Good	Good	Good	Good	Good
Circulation of blood in external coil	Good	Good	Good	Difficult	Good	Difficult	Good	Good
Circulation of saline in pleural cavity	Good	None	Good	Limited to thoracic surgery	Good	Difficult	Excellent	Good
Bath, iced water	Very poor	None	Poor	Fair	Difficult	Poor	Poor	Good
Bath, warm water		None		Fair	Difficult	Poor	...	...
Ice packs	Fair	Poor	Good	Good	Good	Good	Good	Good
Cold or warm air	Good	None	Good	Fair	Fair	Good	Fair	Good
Electric blanket			Good	Good	Good	Good	.	..
Radiofrequency heating			Good	Good	Good	Good	...	..
Large "blankets" for circulation of liquid	Good	Poor	Good	Fair	Good	Good	Fair	Good
Set of "blankets" for circulation of liquid	Good	Good	Good	Fair	Good	Good	Good	Good

The time required for cooling stabilization was 15 minutes. The rewarming rate was 2.3 C/hour. Administration of chlorpromazine controlled shivering and increased the rate of cooling.

The method was used in one patient undergoing surgery for tetralogy of Fallot. Body temperature was 34.7 C before surgery and reached a level of 29.2 C within 25 minutes. The cooling rate was 3.6 C/hour and the rewarming rate, 2.5 C/hour. The patient was also given 50 mg chlorpromazine to prevent shivering. The method was most successful. The chlorpromazine causes the rate of cooling to increase considerably and greatly reduces the need for barbiturates.

► [The ingenious device of hypothermia introduced in 1950 by Bigelow of Toronto, has been used chiefly in cardiac surgery, but undoubtedly it will be found useful in other fields of surgery—Ed.]

**Use of Deep Procaine Injection for Relief of Localized Pain.** Frederick Leet Reichert<sup>9</sup> (Stanford Univ.) reports that injection of 2% procaine into accurately located trigger points has in general brought relief to patients with chronic pain or atypical neuralgia. The pain or neuralgia is due to irritation of peripheral sympathetic fibers in subcutaneous tissue, muscles and fascia of muscles, about blood vessels and in peripheral nerves, attachments of muscles to bony structures and para- and interspinous vertebral ligaments. The atypical neuralgia occurring in headaches, occipital neuralgia, neuralgia of the chest simulating angina pectoris, post thoracotomy neuralgia and sprains along the costal margins and xiphoid furnishes the alarm reaction with stresses that often deplete the adrenal cortex and anterior pituitary glands.

Accurate identification of the trigger areas is important. Deposition of 2% procaine is begun just beneath the skin and made gradually deeper until all trigger spots have been reached. Usually 2.5 cc is injected into each area and not more than 40 or 50 cc is injected at a visit. Hematomas at the injection site are prevented by subcutaneous injection of 10 mg vitamin K before treatment. At least 20 minutes before injection ½ gr phenobarbital is given orally to reduce the toxicity of the procaine. An ampule containing 2 gr sodium phenobarbital should always be available for

(9) Am J Surg 91:699-704 April 1956



intramuscular injection in case of a procaine reaction Adrenal cortex extract, 0.5 cc subcutaneously, is also given

General supportive treatment includes a high vitamin C, high protein diet, multivitamins and minerals, digestive enzymes, suprarenal cortex tablets, potassium, calcium and reserpine Continuance of relief after procaine injection of the trigger points seems to depend on abstinence from alcohol

**Use of "Arterialized" Blood for Determination of Arterial O<sub>2</sub> and CO<sub>2</sub> Tensions** Robert S. Weiner and Philip Cooper<sup>1</sup> (Boston Univ.) believe that determination of arterial O<sub>2</sub> and CO<sub>2</sub> tensions is helpful in evaluating pulmonary function In most such studies, repeated arterial punctures or the use of an indwelling arterial needle to obtain the blood samples is necessary Goldschmidt and Light showed that blood drawn anaerobically from a vein on the dorsum of the hand, which has been heated to 45-47 C for 10 minutes, is equivalent to arterial blood in CO<sub>2</sub> and O<sub>2</sub> content Determination of O<sub>2</sub> and CO<sub>2</sub> tensions on brachial artery blood and arterialized venous blood drawn simultaneously from the dorsum of the hand were carried out under resting conditions in 14 men some normal and some with pulmonary disease Similar studies were done on three others, with blood drawn simultaneously from the brachial artery and a forearm or antecubital vein

The upper extremity was immersed in water for 10 minutes to a point just above the elbow, the temperature of the water maintained at 45-47 C by adding hot water All blood samples were drawn without the use of a tourniquet

The study demonstrated that arterialized venous blood approximates arterial blood in its CO<sub>2</sub> and O<sub>2</sub> tension levels The average determined CO<sub>2</sub> tension in arterialized venous blood was 1.1 mm higher and the average determined O<sub>2</sub> tension was 7.2 mm lower than in arterial blood The difference in O<sub>2</sub> tension of arterialized blood from that of arterial blood is much greater if arterialized blood is drawn from the forearm or antecubital region than from the dorsum of the hand If only the arterialized samples drawn from the dorsum of the hand and corresponding arterial samples are compared the O<sub>2</sub> tension of the arterialized samples is on the average 5.5 mm lower, and the CO<sub>2</sub> ten-

(1) J Thorac & Surg 30:683-686 December 1955

sion averages 1 mm. higher than that in arterial blood.

The study indicates that arterialized venous blood may possibly be used instead of arterial blood in many tests that involve the determination of arterial  $\text{CO}_2$  and  $\text{O}_2$  tensions.

**Evaluation of Rapid Serum Amylase Test** (Fishman and Doubilet) in the surgical emergency ward of Strong Memorial Hospital in all cases of acute upper and midabdominal distress of doubtful etiology is reported by Michel Gilbert<sup>2</sup> (Univ. of Rochester).

**METHOD.**—Amylase activity is estimated in Somogyi units by incubating a small amount of serum with a minute quantity of starch at 40 C. for five minutes. Residual starch, if any, is measured by color changes produced by addition of an iodine reagent. The only equipment needed is a constant temperature water bath, centrifuge, small test tubes, pipets and three dropping bottles.

Of 56 emergency tests, 6 were not checked later by the Somogyi method. Of the remaining 50, 3 did not correlate with the Somogyi test, an error of 6%. Nine (19%) of 47 patients whose amylase levels were correct had definite elevation of serum amylase (over 350 mg./100 ml.). In these patients, acute pancreatitis was diagnosed and treatment was nonsurgical. Further tests were performed later to rule out the possibility that pancreatitis was secondary to some other disease.

The only difficulty encountered with the rapid serum amylase test was with the starch solution, which must be made up every three weeks and kept refrigerated when not in use. Two of the three errors were due to use of old starch solution. Since then, 24 consecutive serum amylase determinations have been without error, when compared with the Somogyi method. The iodine reagent should be changed every four months, to yield sharp color end points.

**Comparative Antigenicity in Guinea Pig of Sutures from Ovine Submucosa and Bovine Serosa** was studied by William R. Sewell and Bradford N. Craver<sup>3</sup> (New Brunswick, N. J.) in an effort to reconcile conflicting reports regarding antigenicity of catgut. Catgut was used in excess of quantities needed in human surgery and was incorporated with a Freund-McDermott formulation highly effective as an adjuvant in stimulating antibody formation by the reticulo-endothelial system.

(2) J.A.M.A. 159:775-776, Oct. 22, 1955.

(3) Ann. Surg. 142:980-985, December, 1955.

Local or humoral antibodies to ovine and bovine catgut could not be demonstrated by intradermal tests, the Schultz-Dale technic or attempts to induce anaphylaxis. The same methods conclusively demonstrated sensitization to ovine and bovine serums. Intradermal tests evidenced existence of hypersensitivity to tubercle bacilli.

Microscopic studies on cellular responses to ovine and bovine catgut implanted in "sensitized" animals indicated weak, approximately equal hypersensitivity to each of these and a cross-antigenic relation between the two. Histologic studies also suggested development of local hypersensitivity to catgut in control animals within 25 days after implantation.

Since materials used were from regular production lots, it is theoretically possible that the slight antigenicity encountered was not an attribute of the collagen per se but of some contaminating proteins. This appears unlikely, however, because rabbits have been sensitized to purified rat collagen.

**Anticoagulant Therapy**, according to Shepard Shapiro<sup>4</sup> (New York Univ.), has been most effective postoperatively in venous thrombosis and pulmonary embolism. Attention is directed particularly to prevention and control of venous thrombosis, to eradicate the source of emboli to the lungs. It is essential that venous involvement be detected as early as possible and, when pulmonary embolism has occurred that it be recognized even in its most obscure form. An acute episode in the chest in the postoperative patient may be due to either pulmonary embolism or myocardial infarction. In either case, therapy with anticoagulants and appropriate supportive measures should be instituted immediately.

Until recently, anticoagulants of choice have been heparin and dicumarol,<sup>®</sup> used to supplement each other—heparin for immediate anticoagulation and to maintain hypocoagulability for 36-72 hours until prothrombin time, prolonged by dicumarol,<sup>®</sup> has reached a therapeutic level. Shortcomings of dicumarol<sup>®</sup>—long latent period and low predictability of prothrombin response—seem to have been resolved by warfarin (coumadin<sup>®</sup>) sodium. Coumadin<sup>®</sup> sodium is the only anticoagulant that can be given intravenously, intramuscularly or orally. Because of the drug's more regular

(4) S. Clin. North Amer. 36:469-483, April, 1956.

effect, it is relatively easy to maintain therapeutic hypoprothrombinemia. It is highly susceptible to counteraction by menadione or vitamin K<sub>1</sub> (mephyton®).

Comparison of properties of currently available anticoagulants (Table 1) with those of the ideal cougulant (Table 2) shows that coumadin® sodium, with one or two doses of heparin, most nearly meets ideal specifications. Heparin and synthetic cougulants are not competitors, they complement each other.

If it is decided that the patient should receive anticoagulants promptly after operation, heparin should be administered after hemostasis is satisfactorily achieved until the long-acting hypoprothrombinemia inducing agent, coumadin® sodium, has become effective. Initial dose of coumadin® is generally 1 mg/kg body weight, minimal dose 50 mg. Patients weighing over 75 kg are given 100 mg. Shapiro prefers to give the first dose intravenously in the same syringe with the first injection of heparin, which is given, 50-75 mg, every four to six hours. Usually, prothrombin time becomes prolonged 12-15 hours after coumadin® is administered, heparin injections are gauged accordingly. Estimation of prothrombin time should be made 24 hours after operation and daily thereafter during the hospital stay. When individual dosage requirement is determined, small doses (6.25-12.5 mg) can be administered over a long period with less frequent prothrombin estimations. Vitamin K<sub>1</sub> (mephyton®) should always be available to counteract hemorrhage. In Shapiro's experience, with use of coumadin®, need for vitamin K has seldom arisen. Adequate protein should be given daily to support liver function during therapy. It is also advisable to administer ascorbic acid, preferably with P' factors to support vascular wall integrity.

Anticoagulants are definitely contraindicated in the following conditions: (1) pre-existing defect in coagulability of blood, hemorrhagic diatheses and all types of purpura, (2) liver disease and nutritional deficiency states in which hepatic insufficiency should be suspected, (3) recent operations on the central nervous system, (4) ulcerative lesions, especially if inaccessible (gastrointestinal tract) or on open surfaces in which hemorrhage may arise, (5) vascular weakness, present or suspected, such as mycotic or "berry" aneurysm or dissection of vascular wall, or (6) renal:



TABLE 1 (Cont)

Advantages	1 Prompt effect 2 Useful in emergencies 3 High predictability of response 4 Ease of control by physician 5 Can be used in presence of nausea vomiting sedation or indwelling tubes	Oval use	1 Oval use 2 Long recovery period helps to maintain a steady effect	1 Oval use 2 Long recovery period 3 Relatively small dose	1 Oval use 2 Short subjects period	1 Prompt induction of hyperventilation <24 hr. 2. Paralyzed when oval used and be used 3. High predictability of response, first, and succeeding doses readily forecast 4. Very sensitive to vitamin K (menadiol or K <sub>1</sub> ) 5. Compatible with heparin for IV or IM 6. With heparin produces immediate and prolonged hyperventilation
Disadvantages	1 Inactive orally 2 High cost 3 Requires frequent injection by trained person and 4 Not suited for long term or ambulant therapy	1 Possibility of side reactions 2 Short recovery period 3 Low predictability of response use 4 Can not be used when patient is sedated or vomiting	1 Long initial period 2 Low predictability of response 3 May be cumulative 4 Cannot be used when patient is sedated or vomiting	As 1 & 2 above	1 Very low predictability of response 2 Difficult to adjust dosage 3 Requires frequent (twice daily) prebromin in de-terminations 4 Short recovery period—tendency to "escape" from therapeutic range 5 Large dose required 6. Cannot be used when patient is sedated or vomiting	No serious disadvantages observed to date

\*Hemorrhage is extension of pharmacologic effect  
†In progress

TABLE 2—HOW AVAILABLE ANTICOAGULANTS COMPARE WITH IDEAL ANTICOAGULANT\*

REQUIREMENTS FOR THE IDEAL ANTICOAGULANT	HEPARIN	PHENINDIONE	DICUMAROL	CYCLODICUMAROL	PTHYL BISCUM ACETATE	WARFARIN SODIUM	REMARKS
1 Oral and parenteral effectiveness	No	No	No	No	No	Yes	
2 Rapid onset of action within one hour	Yes	No	No	No	No	Yes <sup>b</sup>	* Warfarin sodium with heparin IV
3 Wide usefulness (e.g. sedate patients)	Yes	No	No	No	No	Yes <sup>b</sup>	* IV or IM
4 Side effects absent†	Yes	No <sup>c</sup>	Yes	Yes	Yes	Yes	* Blood and cutaneous dyscrasias
5 Cumulative effects absent	Yes	No <sup>c</sup>	Yes	Yes	Yes <sup>d</sup>	Yes	* Tromexan least likely to accumulate
6 Toxicity absent from prolonged use	Yes	No	Yes	Yes	Yes	Yes	
7 Predictability of response	++++	++	++	++	+	+++	* See key below table
8 Uniformity of response from patient to patient	++++	++	++	++	+	+++	
9 Frequency of laboratory tests for initial dosage	Daily	Daily	Daily	Daily	Twice daily	Daily	
10 Control by patient	No	No	No	No	No	No	
11 Cessation of effect when drug is stopped	++++	++	++	++	+++	+++	
12 Cessation of effect by antagonist	++++	++	++	++	+++	+++	
13 Prompt control of overdosage	—	*	*	*	*	Yes <sup>f</sup>	* Excessive hypoprothrombinemia returned to therapeutic range with 0.5 to 2.5 mg KI or 20 mg menadiolone
14 Ability of antagonist (KI) to "treat" excessive hypoprothrombinemia to therapeutic range	—	*	*	*	*	Yes <sup>f</sup>	
15 Capacity to respond after antagonist	+++	++	+	+	++	+++	

\* Adapted and expanded from Goodman, L. S., and Gilman, A., *The Pharmacological Basis of Therapeutics* (2d ed. New York: Macmillan, 1955), and Shapiro S., et al. J. M. Soc. New Jersey, p. 4852, 1951.

† Hemorrhage from excessive dosage is not side effect, it is extension of pharmacologic effect.

‡ These periods can be extended for long range therapy.

++++ = 100%, +++ = High ++ = Medium, + = Low

sufficiency (In two patients with advanced renal failure to whom Shapiro administered dicumarol,<sup>g</sup> response was unusual only in duration of prolonged prothrombin time after each dose, there was no bleeding)

Hemoptysis resulting from pulmonary embolism is not a contraindication to anticoagulant treatment. Rarely is there more than blood-streaked sputum. In any event, risk of fatal embolism is greater than the hazard of hemorrhage.

## NUTRITION

**Clinical Response and Changes in Nitrogen Balance, Body Weight, Plasma Proteins and Hemoglobin Following Tube Feeding in Cancer Cachexia.** M D Pareira, E J Conrad, W Hicks and R Elman<sup>5</sup> (Washington Univ) compared nutritional rehabilitation of 64 patients with advanced cancer with comparably undernourished control patients who did not have cancer to determine whether cachexia of cancer is a primary accompaniment of the disease or a secondary result of anorexia. Standard daily ration administered by tube was 900 Gm (3 500 calories) dry mixture containing powdered whole milk nonfat milk solids, calcium caseinate, dextrose, dextrin-maltose,\* vitamins, iron and choline, furnishing 210 Gm protein (33.6 Gm nitrogen), suspended in 18-24 L water when used as a continuous drip. A more concentrated suspension was used for intermittent instillation (12-15 L water). Additional water was supplied to patients who did not or could not drink to insure adequate urinary output. In the most severely malnourished, continuous drip was used for several days to three weeks or more. During the first two to three days, only half or one-third the standard ration was given, but this was rapidly increased as tolerated.

Hyperalimentation by tube feeding served to break the anorexia-malnutrition cycle in cachectic patients with advanced cancer and to induce weight gain and return of appetite, positive nitrogen balance and regeneration of hemoglobin, as in noncancerous patients. Only in regeneration of serum albumin did cancer patients show possible impairment.

These studies demonstrate that malnutrition itself may beget anorexia and thus perpetuate itself. Progress of malnutrition can be reversed and appetite restored by appropriate tube feeding, which, however, seemed not to affect length of life in terms of tumor growth. Nevertheless, beneficial clinical effect of such feeding was evident in return of appetite, partial return of strength and an increased sense of well being. This led to a happier situation for family and

(5) Cancer 8:803-808 July-Aug 1955



patient, to decreased demands on nursing service and to hospital discharge in a significant number who had been bedridden because of profound asthenia from starvation. Tube feeding is as applicable and vital in management of nonterminal undernourished cancer patients as in those who must have or who have undergone surgery.

► [Pertinent questions about cancer that deserve more investigation are: how does cancer kill its victims?, are there specific toxic factors?, is the anorexia due to such toxic factors?—Ed.]

**Effect of Previous Level of Protein Feeding on Wound Healing and on Metabolic Response to Injury** Doris Howes Calloway, Morton I. Grossman, James Bowman and William K. Calhoun<sup>6</sup> fed protein to male rats at levels of one, two or three times the minimal requirements with calories sufficient to maintain body weight. After 14 days the animals had a uniformly positive nitrogen balance. Control animals were then killed and the others subjected to both a dorsal burn and a 4 cm laparotomy. Recovery was followed for 10 days, during which the groups were subdivided so that in each series one group was fed the same diet as during standardization and a second group the intermediate nitrogen level. The animals were killed on the 4th, 7th and 10th postinjury days. Metabolic response was evaluated by urinary nitrogen excretion, liver composition and adrenal weight, and wound healing by tensile strength measurement and histologically.

Except for urinary nitrogen excretions and liver nitrogen content, none of the criteria detected significant alterations due to the level of protein fed before injury. In the groups preferred the minimal protein level, urinary excretion and hence, negativity of nitrogen balance, were less on the day of injury and first recovery day than in groups preferred the higher levels. The liver nitrogen content was higher at the end of the standardization period in the groups receiving the higher protein intakes than in the group receiving the minimal level.

During the recovery period, feeding higher levels of protein resulted in more positive nitrogen balance and greater total liver nitrogen content than did feeding the minimum requirement, but increasing the level from two to three times the requirement afforded no further advantage. There

(6) *Surgery* 37:935-946, June 1955.

were no differences attributable to variation in protein intake after injury, and none attributable to levels of protein feeding before or after injury in the tensile strength or histologic grading of the wounds.

The maintenance of high protein nutrition before injury is without obvious benefit to the animals in terms of wound healing, as compared with minimal but adequate nutrition.

**Episodic Coma Due to Meat Intoxication as Fatal Complication of Portacaval Shunt in the Human Being.** Meat intoxication is a syndrome, characterized by muscular rigidity, ataxia, loss of function of special senses (particularly vision), stupor, coma and death, originally described in the dog having a portacaval shunt and fed on large quantities of meat. If meat is withdrawn early enough, the animal reverts to normal. McDermott and Adams reported a similar condition in a patient who had episodic stupor, with high blood ammonia levels after a portacaval shunt operation. Henry Leffman and J. Thomas Payne<sup>7</sup> of the University of Washington and the Veterans Hospital, Seattle, report another patient with a portacaval shunt who for 18 months had episodes of varying degrees of clouding of consciousness and confusion.

Man, 48, with side-to-side portacaval anastomosis did well for seven months when symptoms and signs of duodenal ulcer developed. While being treated with frequent milk-cream feedings, banthine<sup>\*</sup> and phenobarbital, he became confused, and urinary retention and weakness of the hands developed. Symptoms disappeared when banthine<sup>\*</sup> was discontinued but did not recur when the drug was reinstated. Similar attacks, with clouding of consciousness, recurred one or two months apart. Later, attacks came oftener, lasted longer and were characterized by deep stupor or coma. No major disturbance of electrolytes or acid base balance was observed. He remained in good general condition despite evidence of progressive chronic hepatic failure. No permanent neurologic deficits developed, and no abnormality of pulse, temperature, blood pressure or respiration was noted. Interval EEG's showed only minor abnormalities. The final episode began after a restless night as stupor which deepened into coma, without icterus, terminating in death three days later. Autopsy revealed more fibrosis but less inflammation of the liver than at operation two years before, with a large duodenal ulcer penetrating the liver bed and evidence of recent gastrointestinal hemorrhage. The portacaval anastomosis was widely patent.

Though banthine,<sup>\*</sup> phenobarbital, arsenic, atropine and paraldehyde were suspected at various times of producing

(7) Am Surgeon 21:488-498, May, 1955.

the toxic effect, no certain drug would induce the toxic state regularly but would be well tolerated for long periods, conversely, episodes occurred at times when all medication had been stopped. Attacks were repeatedly related to intake of milk and cream fortified by protein supplements. The pattern showed apparent spontaneous recovery after the patient became unconscious and received intravenous carbohydrate feedings.

It is postulated that the episodic coma was due to some product of intermediary protein metabolism which the failing liver could neither receive, due to portacaval shunt, nor adequately detoxify, due to disease. Patients with portacaval shunts should receive a high carbohydrate low fat low protein diet and should avoid taking drugs, particularly sedatives which are detoxified in the liver.

Principles of Surgical Nutrition are discussed by Roger D. Williams and Robert M. Zollinger<sup>8</sup> (Ohio State Univ). Basic knowledge of nutrition is important to the surgeon but serves little purpose without careful attention to actual diet intake and weight trend. Day-to-day evaluation of weight should be as routine as that of temperature, pulse and respiration. While emphasis has properly been placed on problems of malnutrition, the equally important factor of obesity is often overlooked. Morbidity and mortality can be lowered by preoperative correction of obesity. Whereas weight reduction may not be practical before many operations, surgeons should refuse elective surgery until some weight reduction has been accomplished, e.g., a 5 ft 8 in man of average build weighing 210 lb should be considered too obese for elective hernia repair or cholecystectomy. Even when obesity is apparent without calculation, comparison with ideal weight helps in planning for preoperative weight reduction and evaluation of excessive eating should be made and charted by the patient. Usually excessive weight is due to fatty tissue alone but mild heart failure or salt retention must be considered.

Correction of nutritional deficits can properly be made only through frequent evaluation of the patient's response and therapy that permits lability in use of several available methods of feeding. Oral intake is preferred and most patients will receive adequate basic requirements if en-

(8) *Am J Clin Nutr* 3:449-455 Nov-Dec 5 1955

couraged through changes of diet and supplemental feedings. Application of a knowledge of protein and caloric content of common staple foods is necessary to attainment of daily requirements. When oral methods fail, tube or intravenous feedings should be instituted. Homogenized milk offers a practical, nutritious and readily available source for both gastric and jejunal feedings.

Because many patients with malignancy or chronic disease cannot await weight gain before operation, blood volume deficits in these patients must be appreciated. These deficits range between 50 and 100 ml whole blood/lb weight lost. The lower figure usually is applicable to uncomplicated cases of jaundice or gastrointestinal cancer, the higher may be encountered in intestinal fistulas or chronic ulcerative colitis. Severe blood volume deficit is found with gastrointestinal bleeding and in patients with chronic weight loss who suddenly increase protein losses due to a complication such as acute intestinal obstruction. In an occasional complicated case or poor risk patient, actual blood volume determinations are required. This is most important in intestinal fistula and in elderly poor risk patients with severe weight loss, particularly with associated heart disease. Despite weight loss, these patients will tolerate surgical procedures if blood volume deficits are corrected.

---

## SHOCK, FLUIDS AND ELECTROLYTES

Septic Shock W. A. Altemeier and William Cole<sup>9</sup> (Cincinnati Gen'l Hosp.) review 93 fatal cases of septic shock seen between Jan 1, 1951 and Nov 16, 1955. Types of infection producing shock were peritonitis, 50 cases (54%), intra abdominal abscess with peritonitis, 11 (12%), infections of abdominal wall and perineum, 17 (18%), cellulitis of skin and subcutaneous tissues, 5 (5%), and miscellaneous conditions 10 (11%). Bacteremia was proved in only 11 of 26 cases in which blood cultures were taken, 6 showed hemolytic *Staphylococcus aureus*. In most cases, cultures of areas of infection demonstrated mixed infections. Sur-

(9) Ann Surg 143 600-607, May 1956

vival after diagnosis of hypotension and shock varied from  $\frac{1}{2}$  hour to 216 hours (average, 47 hours) Autopsies, performed in 64 cases, were not informative Pulmonary edema was present in 16 and lower nephron nephrosis in only 5 In six, the adrenals were involved, with acute degeneration in two and massive hemorrhagic infiltration in one

The correct clinical diagnosis of septic shock was made

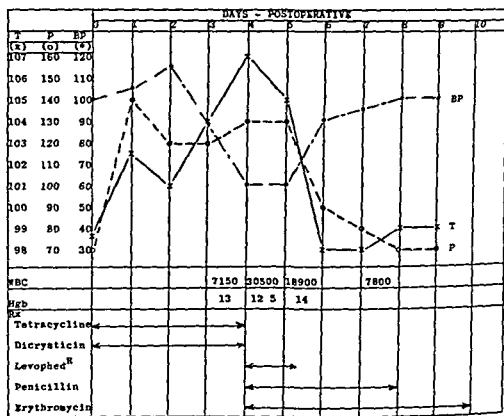


Fig 6—Course and response to early recommended treatment for septic shock. (Courtesy of Altermeier W A and Cole W Ann Surg 143 600-607, May 1956)

infrequently Inability to diagnose septic shock appears to be due to ignorance of the possibility of this complication during an infection and to unfamiliarity with its symptoms and signs

Diagnostically helpful signs are (1) sudden insidious development of unanticipated hypotension and other symptoms of circulatory collapse in a patient with fever, (2) occurrence of shock in absence of hemorrhage or trauma, (3) serious infection, the presence of which may be obscured by masking of localizing symptoms by antibiotics,

(4) signs of vegetative endocarditis; (5) failure of shock to respond to usual treatment, (6) a high white blood cell count, usually 20,000 or more, with marked predominance of polymorphonuclear leukocytes and evidence of toxic granulation (a very low white blood cell count may also suggest overwhelming infection), (7) sudden signs of shock in a patient with known intra-abdominal abscess, and (8) petechiae, unexplained delirium or icus

Treatment was aimed primarily at restoration of blood pressure by infusions Levophed,\* used in 45 cases, elevated blood pressure temporarily in all Antibiotics, used in 89 cases, were obviously incorrectly chosen or inadequate Cortisone should be useful as a supportive measure until septic lesion can be controlled by surgery and intensive antibiotic therapy

Figure 6 illustrates the effectiveness of early diagnosis and treatment in the management of a patient with severe staphylococcic hemorrhagic enterocolitis and septicemia, secondary to terramycin\* therapy Similar treatment was used successfully in six other recent cases

Factors apparently concerned with development of septic shock include hemoconcentration with diminished blood volume, disparity between blood volume and volume of peripheral circulation caused by diffuse vasodilatation, circulatory failure due to a profound toxemia and direct toxic effect of infection on the adrenal glands

► [This is a very important condition which, as the authors state, is not generally known and is seldom recognized—Ed]

Shock, particularly hypovolemic shock due to surgical or traumatic wounds, burns, tourniquets, crush injuries and hemorrhage, is discussed by Jonathan E Rhoads, William S Vaun, William M Parkins, Max Ben and Harry M Vars<sup>1</sup> (Univ of Pennsylvania) New information being added to knowledge of shock necessitates some rearrangement of emphasis The role of bacteria, probably intestinal, in the pathogenesis of hemorrhagic shock is indicated by the improvement in survival rates found by Fine and associates with the addition of oral polyvalent antibiotics Pre-treatment was necessary for best results Differential cooling studies indicate that in shock caused by cutting off the circulation in the lower thoracic aorta, direct cooling

(1) S Clin North America 35 1585 1595, December 1955

of the intestine by peritoneal lavage with cold saline was effective in increasing tolerance to this type of ischemic shock. Other experiments indicate that shock, in turn, decreases capacity of the animal to clear his blood stream of injected organisms and to clear his organs of contamination.

Regardless of initiating cause, a chain reaction is set up in hypovolemic shock whenever shock reaches a sufficiently severe degree. Once this has begun to operate, therapy must be swift and abundant if the process is to be reversed. If it is not reversed promptly, further therapy is usually of no avail and death is imminent.

In treatment, it is important to relieve pain and fear and to provide rest in a temperate environment, avoiding extremes of heat or cold. The importance of the head-down position in improving circulation to the brain has been substantiated. Inability to stand position changes from horizontal to vertical without faintness or a drop in blood pressure is often a good index of so-called pre-shock. Increasing circulating blood volume remains the cornerstone in treatment of hypovolemic shock. It is best accomplished with suitable whole blood, and this may be universal donor blood with a low titer of agglutinins in the plasma. Cross-matching should be done. In the absence of whole blood plasma stored at room temperature for six months or longer, dextran, P-20 gelatin or polyvinylpyrrolidone may be effective. When these are used it is imperative to obtain hemostasis, otherwise their effect will be largely to wash red cells out of the circulation.

Although chlorpromazine may reduce the amount of blood lost before blood pressure falls to a critical level and, in animal experiments, may increase tolerance to a given hypotensive blood level, it is highly dangerous in a patient who is already in shock. The authors advise against its use unless satisfactory evidence of its effectiveness under appropriate controlled conditions can be shown.

The place of nor-epinephrine is difficult to define. There is no doubt that, given intravenously at a suitable rate, it has a profound capacity to raise blood pressure, presumably mostly by concentrating circulation in restricted areas. Its use should be restricted to brief periods when nothing else is available and to cases in which rapid administration

of whole blood in liberal amounts fails to elevate blood pressure above shock levels. It should not be a substitute for transfusion.

**Intra-arterial Transfusion: Artificial Oxygen Saturation of Preserved Blood:** Demonstration of Apparatus is presented by A. Berner and L. Hollender<sup>2</sup> (Strasbourg, France). Intra-arterial transfusion is often a lifesaving measure, especially in shock in which there is pronounced venous and pulmonary stasis. A rapid, massive intravenous transfusion in such cases exaggerates the circulatory difficulty, but intra-arterial transfusion may bring about striking recovery. Apparatus for intra-arterial blood transfusion must permit a known volume of blood to be administered under controlled pressure, which obviously must be higher than the existing intra-arterial pressure; in most cases 100-300 cc. blood/minute is required.

All modern intra-arterial blood transfusion apparatus arterialize blood according to the same principle. The authors' setup consists of a somewhat modified Merke flask. Internal pressure is produced with oxygen instead of air and is controlled manometrically. Oxygen is conducted into the blood at the bottom of the flask. Positive pressure is controlled by a stopcock at the outlet tube. Blood can be transfused through this large tube to the patient. The Merke flask is refilled during transfusion through a funnel mounted on the top.

Tests of oxygen saturation of blood in this apparatus proved disappointing. Oxygen content increased from only 28.4% to 62.8% after arterialization for 15 minutes with 500 cc. oxygen/minute. At this rate, satisfactory oxygenation would require 30-45 minutes. For this reason, Nikitin's method of arterialization using hydrogen peroxide was combined with use of the apparatus, which is effective in regulating injection pressure.

In performing intra-arterial transfusion, factors are blood quantity as required, usually 500-1,000 cc., and transfusion rate, 100-250 cc./minute. With a large cannula, this rate is easily attained with apparatus pressure of 100-150 mm. Hg, produced with an oxygen stream of 200-300 cc./minute, with careful regulation of pressure by the stopcock of the

(2) *Helvet chir acta* 22 333 335, November, 1955



outgoing tube Venous blood can be completely arterialized (oxygen saturation of 98.2%) in less than one minute by addition of 0.7 cc of 30% hydrogen peroxide

**Antihistaminic Drugs in Treatment of Nonhemolytic Transfusion Reactions** were studied by C. Ronald Stephen, Ruth C. Martin and Michel Bourgeois-Gavardin<sup>3</sup> (Duke Univ.) Allergic and anaphylactic reactions to blood transfusion are regarded as sufficiently serious to stop the administration of blood. In some instances, life may be endangered from severe shock associated with the reaction.

Probably the most frequent type of reaction to transfusions is pyrogenic. Although the least noxious of transfusion reactions, it may cause subjective discomfort and apprehension and give cause for alarm in the seriously ill patient.

For about a year, all adults who received blood transfusions in Duke Hospital were followed carefully, all types of reactions being noted. Just before administration of the first bottle of blood to each patient, 25 mg tripeleennamine (pyribenzamine®) was added to the blood under sterile conditions. It was not added to subsequent bottles unless the patient received more than 12 bottles or there was more than a six hour interval between transfusions. Control patients, not given tripeleennamine, were followed at the beginning and end of the investigation.

Reactions attributable to circulatory overloading or to transfer of the virus inducing hepatitis were not specifically noted in the study. Among the controls there were 89 'pyrogenic' reactions in 72 patients, only 5 of the reactions were noted during surgery or in the recovery room post-operatively. Among patients receiving tripeleennamine with the first bottle of blood, there were 55 reactions in 45 patients, the fewer number of reactions being statistically significant. Among the controls there were 47 allergic type reactions in 47 patients; among the tripeleennamine treated group 11 in 10 patients.

Tripeleennamine in drug dosages that are considered clinically safe significantly reduces the incidence of pyrogenic and allergic type reactions.

**Parenteral Fluid Therapy of Burns during the First 48 Hours.** J. Frederick Eagle<sup>1</sup> (Univ. of Buffalo) states that the most important lifesaving factor in the therapy of severe burns during the first 24 hours is proper use of parenteral fluids. A single solution containing two-thirds normal saline, 5% glucose and 2% serum albumin in amounts equal to 30 cc./sq. m./percentage body burn plus an amount equal to 10% of the body weight in kilograms plus 4,000 cc./sq.

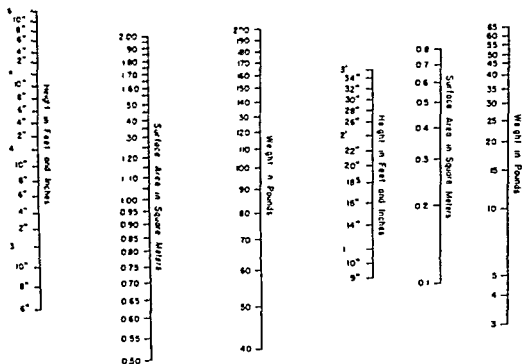


Fig. 7—Surface area nomograms (Du Bois) (Courtesy of Eagle, J. F. New York J. Med. 56 1613 1618, May 15, 1956)

m. for the first 48 hours is recommended. Extreme caution should be used toward the end of the second day. The amount of any whole blood given should be subtracted from the calculated figure. The plan of treatment and the nomograms for determining the surface are shown in Table 1 and Figure 7. A sample case for determining the water, protein and electrolyte losses in the first 48 hours is shown in Table 2.

The use of a formula is only an approximation at best and depends on other approximations, the most variable of which is probably the estimation of the extent of burn. It is necessary to watch the patient very closely and to modify the program depending on the clinical situation. One method

(4) New York J. Med. 56 1613 1618, May 15, 1956

is to measure the urine output, preferably hourly and with a catheter in place, an output between 25 and 40 cc/hour is ideal. Another laboratory technic is the use of hourly hematocrit readings.

TABLE 1—PARENTERAL FLUID THERAPY FOR BURNS

1 Composition of Fluid A two thirds normal saline solution with 5% glucose and 2% protein. This may be prepared by mixing 2 parts of 5% glucose in normal saline with 1 part of 5% glucose in water, and adding 2 Gm of concentrated serum albumin to each 100 cc of solution.

After being assured of adequate urine output, 1.5 Gm potassium chloride should be added to each liter of fluid. This can be most easily done by adding the contents of a 10 cc ampule of 15% potassium chloride to each liter of fluid.

2 Rate of Administration

a) 30 cc/% body burn/sq m in first 48 hours to replace loss through the burn, plus

b) 10% of the body weight in kg in the first 48 hours to replace loss from the blood volume into the interstitial tissues, plus

c) 2,000 cc/sq m in 48 hours for insensible water loss, plus

d) 2,000 cc/sq m in 48 hours for urine production

3 Subtract from the above figures any blood that is given and do not give more than 3-4 cc/kg body weight

4 In burns greater than 50%, assume a burn of only 50%. In burns of less than 15%, do not administer the fluid equivalent to 10% of the body weight in kg

5 Give one third of this calculated amount of fluid in the first 8 hours after the burn, one third in the following 16 hours, and one third on the second day

Example Assume a 30 kg boy with a surface area of 1 sq m has incurred a 50% body burn

Then  $30 \times 50 \times 1 = 1,500$  cc in first 48 hours to replace loss through the burn

$30 \times 0.1 = 3,000$  cc in first 48 hours to replace loss into tissues

$2,000 \times 1 = 2,000$  cc in first 48 hours for insensible water loss

$2,000 \times 1 = 2,000$  cc in the first 48 hours for urine production

8,500 cc total

One third of this total, or 2,833 cc should be given in the first 8 hours after the burn. 2,833 cc in the next 16 hours, and one third during the second 24 hours

6 Follow the urine output carefully and adjust the rate of infusion so that the patient voids between 10 and 40 cc/sq m/hour

7 If hourly hematocrit determinations are done, a 1% increase in hematocrit above 45 indicates a 2% decrease of blood volume. In the following hour this diminished volume must be restored by speeding up the infusion by an amount equal to 2% of the blood volume (which is 0.14% of the body weight) plus an equal amount to take care of this increased continuing rate of loss. A 1% fall in the hematocrit below 45 represents a 3% increase in blood volume (which is 0.2% of the body weight in kg), and the infusion must be slowed in a similar manner

► [The treatment of recent burns still constitutes one of the major surgi

TABLE 2—WATER PROTEIN AND ELECTROLYTE LOSSES IN BURNED PATIENTS IN THE FIRST 48 HOURS

TYPE	AMOUNT IN 48 Hr		COMPOSITION	
	30 cc/sq m / % body burn	10% body weight in kg	1% sodium, 3.5% protein	1% sodium, 3.5% protein
Loss of serum through burn				
Loss of plasma as edema				
Insensible water loss	2000 cc/sq m		Plain water	
Urine water loss	2000 cc/sq m		0.6% sodium	

WATER PROTEIN AND ELECTROLYTE LOSSES CALCULATED FOR A 30 kg 1.50 M PATIENT WITH A 50% BODY BURN				
	Water (cc)	Sodium (gm)	Protein (Gm)	
Loss of serum through burn	30 × 1 × 50	1500	15 (1%)	52.5 (3.5%)
Loss of plasma as edema	30000 × 0.1	3000	30 (1%)	105 (3.5%)
Insensible water loss	2000 × 1	2000	0 (0.3%)	0
Urine water loss	2000 × 1	2000	0	0
Totals to be replaced		8,500	58 (0.6%)	157.5 (1.85%)

This is essentially a two thirds normal saline solution with 2% protein. Similar calculations on patients of varying sizes and with burns of varying extent demonstrate that the range of saline concentration varies between 0.54 and 0.71%, and the range of protein concentration varies between 1 and 2%.

cal problems According to my colleague and successor as Head of the Department of Surgery at Washington University, Dr Carl Moyer, an exhaustive review of the literature shows that there has been practically no reduction in the mortality of severe burns in the past 100 years—Ed]

**Inhibition of Prothrombin Activation with Dextran** was studied in vitro by Walter H Seegers, Walter G Levine and Shirley A Johnson<sup>5</sup> (Wayne Univ) in an attempt to elucidate the mechanism for clotting disturbances associated with use of dextran reported in some experimental studies Dextran, in suitable concentration, may inhibit threone activity, which arises from combined action of platelet factor 3 and plasma platelet cofactor I, demonstrated with use of purified prothrombin as a substrate Formation of threone activity and its subsequent participation in activation of purified prothrombin together with calcium and Ac-globulin may be represented by the following equations

(1) Platelet cofactor I + PI factor 3 = threone

(2) Prothrombin  $\xrightarrow[\text{serum Ac globulin}]{\text{Ca}^{++}, \text{threone}}$  thrombin

Inhibition of threone activity by dextran can be overcome completely by adding a small amount of purified thrombin to the reaction mixture containing purified prothrombin calcium ions, platelet cofactor I platelet factor 3 and Ac globulin It seems likely that the role of thrombin in overcoming dextran inhibition is concerned with formation of a derivative of prothrombin A number of other polysaccharides may also inhibit threone activity and presumably the formation of a derivative of prothrombin

Concentration of dextran effective for inhibition in these experiments is within range one could expect to find when this plasma volume expander is used clinically It is not certain that bleeding tendencies occasionally observed with use of dextran occur following inhibition of threone but the information is adequate to account for clinical observations related to bleeding Great ease with which small amounts of thrombin nullify the inhibition strengthens this opinion Small concentrations of thrombin can be obtained by several mechanisms in normal clotting of blood then inhibition with dextran would be completely overcome and

thus would account for the fact that difficulty with dextran is rare clinically. In those few cases in which a bleeding tendency develops this small thrombin concentration perhaps does not build up because the particular patient is more dependent on ability to develop thrombin activity than the average person.

**Efficacy of Dextrans of Different Molecular Weights in Shock Secondary to Limb Clamping** is evaluated by Lorraine C. Smith and R. E. Haist<sup>6</sup> (Univ. of Toronto). Traumatic shock produced in rats by removal of metal clamps which had been applied to both hind legs for 10 hours was lethal within 24 hours to all animals not receiving fluid therapy. Infusion of plasma expanders delayed or prevented development of irreversible shock. All fluid therapy relieved oliguria produced by shock though relief generally occurred 24 hours after release of the clamps. Incidence of survival with dextran solutions was increased with increasing molecular weights. This seemed to be related to retention of larger molecules for a longer time within the body. The plasma expander which best promoted survival was the Connaught dextran 13-1, a solution with an intrinsic viscosity of 0.34 (mean molecular weight 150,000).

Results are difficult to compare with those of other investigators because of different molecular weights of the substances used, different dosages, rates and times of infusion and different methods of measuring dextran excretion. However, the findings agree essentially with those of authors who have reported an inverse relationship between the amount of dextran appearing in urine and the molecular size of preparations infused.

**Hazards of Blood Transfusion** are discussed by Julius R. Krevans<sup>7</sup> (Johns Hopkins Univ.). Whole blood transfusions are of value in the management of elective surgery and are irreplaceable in treatment of medical and surgical hemorrhagic catastrophes. Each transfusion, however, is accompanied by the hazard of an untoward reaction, which may lead to death. Transfusions are inadvisable except when a valid need exists.

Mechanical factors may cause reactions. Rapid infusion

(6) *Canad J Biochem & Physiol* 33 553-561, July, 1955

(7) *Postgrad Med* 19 41-44, January, 1956

of blood may cause pulmonary edema, especially in patients with cardiac disease. Some patients should be given only packed red blood cells. The "pumping" of blood may lead to air embolus. Hypersensitivity reactions may be due to some allergic substance in the blood, the simplest and most frequent, occurring soon after transfusion has been started, consists of itching, urticaria and occasionally angio neurotic edema. There may be rise in temperature. Symptoms usually are not serious, are self-limited and respond to epinephrine or antihistamines. Some reactions may be more serious, causing bronchospasm. Delayed reactions consist of fever, joint pains and swelling and malaise. Râles may develop in the lungs. Cortisone and hydrocortisone are helpful.

Reactions may be caused by agents accidentally transmitted during transfusions. Malaria, relapsing fever, syphilis and other infections may be transmitted by donor blood. Careful screening of donors and the serologic test for syphilis prevent these reactions. The most serious and common problem is transmission of hepatitis. Hepatitis is caused by a virus and occurs in about 1 in 300 transfusions. Serious reactions may be caused by bacteria in donor blood. The reaction usually begins with a shaking chill and rise in temperature, followed by abdominal pain, nausea and vomiting and diarrhea. Severe hypotension often occurs. Therapy includes broad spectrum antibiotics, nor epinephrine and corticoids. Common pyrogenic reactions, due to presence of sterile bacterial products in the anticoagulant solution or the transfusion equipment may occur.

Despite improvement in technics for typing and cross matching hemolytic reactions occur usually because of mechanical errors in labeling or transcription or in administering blood to the wrong patient. Cross matching procedures using protein mediums and the indirect Coombs technic have helped to eliminate hemolytic reactions due to unusual antibodies in the recipient. When a patient receives incompatible blood the clinical picture can vary from little or no change to a rapidly fatal reaction. A typical moderately severe reaction starts with malaise, restlessness and perhaps headache and backache. A shaking chill and rise in temperature follow. Abdominal symptoms and hypotension may appear. Sometimes hemorrhagic diathesis may occur.

Hemolytic transfusion reactions are confirmed by demonstrating hemoglobinemia and hemoglobinuria and by re-examining the blood types and cross matching. If the patient survives the initial insult, proper management of the acute renal failure can prevent death.

"Plasma transfusion reaction," seen in patients requiring repeated transfusions over a long period, is characterized by a febrile reaction and failure to demonstrate expected increase in number of red blood cells. The reaction can be ameliorated or prevented by removing the plasma and washing the red blood cells before transfusion. Corticoids are used for treatment. Hemorrhagic diathesis, mainly due to thrombocytopenia may follow rapid transfusion of large quantities of blood.

**Effect of Magnesium Sulfate on Alterations in Renal Dynamics Induced by Intravenous Hemoglobin.** Of various explanations offered as to the etiology of renal damage following transfusion reactions or severe acute hemolytic states the most plausible seems that hemoglobin exerts a vasospastic effect. William J. A. Demaria and Jerome S. Harris<sup>8</sup> (Duke Univ.) report a study on dogs directed toward reproducing that phase of a transfusion reaction which could record the lysed cell effect without the shock state usually associated with transfusion reaction. After the pattern of response was established, the effect of the vasodilator,  $MgSO_4$ , was studied during constant infusion of the lysed cells.

Introduction of large amounts of lysed red blood cells intravenously can cause a significant lowering of glomerular filtration rate (GFR) and effective renal plasma flow (ERPF), with associated fall in urinary output. These effects are manifest only while infusion of lysed cells is proceeding. On stopping the infusion, measurements revert to normal control levels despite the presence of high levels of free circulating hemoglobin. The actual level of hemoglobin concentration seems less important in causing these changes than the rate at which the level is achieved.

When  $MgSO_4$  is introduced during lysed cell infusion, the changes promptly revert toward or to normal. If a satisfactory level of serum magnesium is established before



change in function as measured by clearance technics

These results make it difficult to consider that the renal effect of lysed cells or hemoglobin is solely secondary to obstruction of renal tubules by precipitation of hemoglobin or cell stroma derivatives. It is unlikely that  $MgSO_4$  solution could immediately repair a toxic action by hemoglobin or cell stroma on renal tubule cells. It is highly probable that vasoconstriction secondary to lysed cells is the primary mechanism responsible for diminishing GFR and ERPT, since the vasodilator action of  $MgSO_4$  immediately reverses this change.

Vasoconstriction phenomena probably play a definitive role in causing renal damage during a transfusion reaction and it is likely that the effect would be more serious when superimposed on the anaphylactic shocklike phase present in most such reactions. However, it is quite conceivable that renal damage could be caused by massive hemolysis unaccompanied by shock. These studies indicate that use of a known vasodilator drug immediately following such occurrences may be of considerable value.

---

## WOUNDS AND WOUND HEALING

**Influence of Temperature on Surface Bleeding** **Favorable Effects of Local Hypothermia** Vallee L. Willman and C. Rollins Hanlon<sup>9</sup> (St. Louis Univ.) produced a diffusely bleeding surface by removal of split thickness skin grafts in anesthetized dogs. When the rate of bleeding from such lesions was observed after application of moist gauze compresses at temperatures varying from 5 to 65 C, the blood loss appeared to be less with compresses at lower temperatures. A shift from high to low temperature decreased the rate of bleeding and a shift from low to high temperature increased it.

Hot applications to control diffusely bleeding surfaces are not only inefficient but may be dangerous. The precise nature of hemostasis remains obscure and relative roles of coagulation and blood vessel response to injury are not settled. The contractility of the capillaries during cooling has

been demonstrated experimentally. Alteration in the reactivity of vessels under the influence of heat is less well substantiated. Experimental studies indicate that blood coagulability is decreased when the temperature rises.

► [There is no doubt that much harm has been done to tissues by the indiscriminate use of hot packs. How often does one see a surgeon place in the abdominal cavity packs so hot he can hardly handle them despite the protection afforded his hands by rubber gloves? The anesthetized patient cannot complain.—Ed.]

**Tetanus: Summary of 32 Cases with Special Reference to Prevention** is presented by Victor A. Gilbertsen and Stuart W. Arhelger<sup>1</sup> (Univ. of Minnesota). Ages ranged from 20 months to 81 years, half the patients were 16 or younger, and mortality in this group was 25%. Of nine patients over 50, six (67%) died. The time interval from injury to first symptom varied from 3 to 23 days. An initial injury was apparent in 30 patients. Initial symptoms included trismus, spasm of dorsal muscles, extremity muscle spasm and influenza-like onset. Onset with trismus was most common, 19 (60%) patients were so affected, and 7 of these later died from the disease. Patients with spasm of the dorsal muscles usually noted spasm, pain or tenderness of the back or cervical muscles, which occasionally progressed to opisthotonus. Two of six patients so afflicted died. One of four patients who presented spasm of the extremity muscles died. Among three patients with influenza-like onset, no deaths occurred.

Several of the injuries followed by tetanus were grossly clean wounds or were so cleansed as to seemingly remove any contamination. Possibly, these wounds were free from tetanus organisms at time of original injury but were contaminated before healing occurred. Pneumonia and atelectasis were the outstanding findings at autopsy.

It seems that the battle casualty and the newborn child have been replaced as victims of tetanus by the man in the barnyard and the child on the farm. Besides debridement and cleansing of wounds, protection from contamination before healing has occurred appears important. The usual prophylactic dose of 1,500 units of tetanus antitoxin was inadequate to prevent development of the disease in several patients. It is suggested that this dose be increased to 5,000 or 10,000 units when there is a likelihood of presence of

(1) Minnesota Med. 38:393-396, June 1955.

tetanus spores Current fatality rates (31% in this series) emphasizes the need of routine immunization with tetanus toxoid, which should probably include both children and adults

► [Certainly nobody could disagree with the conclusions of the authors that more people, especially children, should be immunized with tetanus toxoid See the following two abstracts—Ed]

**Persistence of Antitoxin Levels after Tetanus Toxoid Inoculation in Adults and Effect of Booster Dose after Various Intervals.** Joseph M Looney, Geoffrey Edsall, Johannes Ipsen, Jr, and William H Chasen<sup>2</sup> (Boston Univ) determined the tetanus antitoxin titers in 144 veterans of World War II at intervals of 1-10 years after their last injection of tetanus toxoid After injection of booster doses of fluid or alum precipitated toxoid, samples of blood were titrated at 6, 14 or 21 days or 1 year later Antitoxin titrations showed that the levels of antitoxin were statistically identical in groups arranged according to intervals since last toxoid injection The over-all geometric mean titer was 0.34 unit/ml Of the 144 subjects, 35 had less than 0.08 unit, and 14 had less than 0.025 unit/ml Of 102 subjects tested six days after the booster dose, 98 exhibited titers above 0.08 unit/ml Of the four remaining, one had no later test, one had less than 0.2 unit after 14 days and 0.025 unit after 1 year, and two had titers above 0.2 unit a year later All of 76 subjects with titers determined two or three weeks after a booster dose had levels above 0.1 unit/ml

All but 1 of 68 subjects whose blood was titrated a year after booster injection showed titers above 0.1 unit/ml and 10 subjects exhibited levels between 0.1 and 0.5 unit This range may be adequate, as studies by others suggest that after a year has elapsed since a booster injection, the subsequent drop is much slower than the fall during the first year Of 130 subjects on whom clearly interpretable post-inoculation titers were obtained, 129 were demonstrated to respond to tetanus toxoid injection The ability to respond was unrelated to the time elapsed since the last toxoid injection

Booster doses of tetanus should be administered routinely at fairly regular intervals, and four year intervals seem satisfactory A routine booster at any time up to 10 years

may restore immunity, and a booster dose of tetanus toxoid can be relied on in an emergency in any fully immunized person up to 10 years after the last previous toxoid injection. However, in the event of multiple, extensive or heavily contaminated injuries, especially of the head or neck, uncertainty regarding previous tetanus immunization or delay in administering the emergency booster injection, the simultaneous administration of antitoxin with toxoid is justified.

Current Therapy of Tetanus is described by Harry W. Hale, Jr., and John F. Weisknar<sup>3</sup> (Buffalo). The diagnosis of tetanus is based on a history of recent injury, with the characteristic picture of painful rigidity of the muscles of mastication and inability to open the mouth with hyperactive reflexes, followed soon by spasm of the neck muscles and later by spasm of the back and abdominal muscles and muscles of the extremities, and generalized convulsive seizures. The sensorium remains clear except in periods of hypoxia due to convulsions.

The patient should be skin tested to the antiserum and, after desensitization, if necessary, given 40,000 units intramuscularly and 40,000 units intravenously. An additional 10,000-20,000 units should be injected locally about the wound before operative manipulation. Subsequently, antitoxin should be given intramuscularly in 10,000-20,000 unit daily doses for five to seven days. The wound should be excised or debridement done.

Tracheostomy may be necessary when severe spasm of the muscles about the face, throat and neck causes difficulty in swallowing, coughing and clearing secretions from the respiratory passages. Barbiturates, chloral hydrate and paraldehyde are used as necessary in large doses to control convulsions. Although muscle relaxants such as curariform drugs have been used, they are not generally needed. The patient should be kept in a quiet, darkened room and protected from stimulation as much as possible. An indwelling catheter is usually necessary. Liquids may be given through an indwelling gastric tube. Antibiotics are used primarily to combat respiratory infection.

Although passive immunization with 1,500-3,000 units of antitoxin as prophylaxis will reduce the risk of tetanus for

10-14 days, the incidence of reactions is high. Antitoxin in a person sensitized to the vehicle serum should not be used prophylactically. The immunity established in service personnel was found to be still effective 10 and more years later. All showed an accelerated response to a booster dose of toxoid, with sharp rises in circulating antibodies in four to seven days. This information, together with the fact that the incidence of reactions to toxoid is extremely low, makes a strong case for an active immunization program among adults. Booster injections of toxoid should be given to all previously immunized persons not more than five years apart. Although some physicians have given the antitoxin and toxoid at the same time, it is best to wait two or three weeks after passive immunization before starting a course of active immunization with toxoid. Toxoid immunization should be carried out after recovery from clinical tetanus, since the latter does not confer immunity.

**Heroic Therapy of the Most Severe Cases of Tetanus—Maximal Curarization without Anesthesia, but with Tracheostomy and Artificial Respiration: First Four Cases treated by this method are reported by Pierre Mollaret<sup>4</sup> (Paris).** Artificial respiration is carried out with the Engström apparatus, with repeated control of pH, CO<sub>2</sub> tension and oxygen content of blood. With this technic, massive doses of curare can be given until tetanus spasms disappear. General anesthesia is omitted because it carries high risk if continued for a long period and is unnecessary if curarization is prolonged sufficiently. Potentiating drugs are used only in small quantities. Penicillin is given to control local infection, and massive doses of tetanus antitoxin are administered.

Woman was hospitalized for treatment of tetanus after attempted abortion (although no pregnancy had existed). All symptoms of severe disease were present: uterine port of entry, short incubation period (five to six days), rapid onset of trismus, dysphagia and generalized spasms, fever, tachycardia and tachypnea, which became worse by the hour, accompanied by signs of suffocation. Massive doses of curare (total 1,322.5 mg. d-tubocurarine) were given continuously by intravenous drip for 10 days, with tracheostomy and artificial respiration with the Engstrom respirator. No anesthesia and only very small doses of classic sedatives were given, i.e., 225 mg. chlorpromazine, 275 mg. phenegan,<sup>®</sup> 1.2 Gm. phenobarbital, 12 Gm. chloral hydrate and 18 Gm. calcium bromide. A single in-

(4) Deutsche med. Wchnschr. 81 365-370, Mar. 16, 1956.

jection of 250,000 units of antitetanus serum, daily doses of 5 000,000 units of penicillin and 1 Gm streptomycin were given. Improvement was rapid after the 10th day with agranulocytosis the only complication. This required treatment for several weeks with cortisone. It was not determined whether tetanus toxin medication, blood transfusion or serum reaction caused the complication.

Other authors who have used curare in treatment of tetanus have combined it with other therapy, such as anesthesia. Mollaret emphasizes the simplicity of his method and comments that there are no longer incurable cases of tetanus, barring unforeseen complications and incurable co-existing disease.

**Burns in Children** are all preventable, barring general disaster, according to Harvey S. Allen and Sherman W. Day<sup>5</sup> (Northwestern Univ.). Age, thin skin and modus operandi of burns in children lead to differences in type and surface distribution from those in adults. Scalds on scalp, face, neck, shoulders and upper trunk are common as a result of overturning hot liquids from stove or table. Scalds of feet and buttocks occur from bathing in tubs heated on the stove. Thermal accidents involving feet often occur from the child's going barefoot. Children also are vulnerable to severe, full thickness flame burns when clothing becomes ignited. Hand burns often involve the palm, from grasping hot objects. Mangle burns, involving the dorsum, are accompanied by crush injury. The small infant may be burned seriously by direct contact with hot water bottles placed next to the skin to provide warmth. Burns caused by spilling contents of a steam inhalator are dangerous, because to the usually severe burn is added the hazard of pre-existing upper respiratory infection.

Prevention is ideal, but with trauma the main emphasis must be on treatment. Burns produce open contaminated wounds of variable depth, capable of causing shock. The therapeutic objective is to achieve a clean closed wound at the earliest date with the least residual disability. The general plan of hospital care is to treat the local wound and systemic reaction immediately and simultaneously. The thin skin of the child may be damaged more seriously than first appears. The ratio of surface area to blood volume is less than in adults, and children may evidence shock with burns of far less than 25% surface area.

Shock is energetically and aggressively managed. Reduced circulating blood volume, with its accompanying thirst, is combated by use of plasma, whole blood or a plasma expander. As circulation is improved by parenteral therapy, generally in 10-12 hours, oral intake can be begun cautiously. Whole blood is the ideal replacement because it also provides vital oxygen-carrying red cells to replace those damaged by the burn and hemoconcentration. Management of shock with lung burns is more difficult, since pulmonary injury leads to edema, requiring caution in intravenous therapy. In such cases, fluid intake should be kept a little less than the calculated optimum. Râles or wheezing usually call for decrease in intravenous fluids.

Depth of burn is difficult to predict on initial inspection, and accurate estimate can be made only at first dressing change, about the fifth postburn day. Slough of a full thickness burn should be removed by surgical excision when demarcation is definite and whenever the patient's general condition warrants operation under general anesthesia. Persistent shock, poor nutrition, upper respiratory infection or other complication contraindicates surgery. Face and neck wounds sequestrate rapidly because of excellent blood supply, and hence are never excised.

Grafting can be done two or three days after excision of slough, after re-evaluation of general condition. If daily dressing has been used to remove necrotic tissue, grafting can be done as soon as dead tissue is no longer present. If nutrition is good, immobilization adequate and infection absent, takes of grafts are good. When donor skin is insufficient to allow complete closure at initial operation, donor sites must be reused, after two to four weeks of regeneration.

The ideal of early initial treatment with continuity of care until final rehabilitation does not always prevail. Many children with burns are brought to the hospital 48 hours to many months after the accident. Late cases nearly always show some infection, often with copious, foul-smelling wound discharge. Patients have persistent fever and eat poorly. Many have become dependent on opiates for sedation. These cases are nutritional emergencies and the state must be corrected rapidly by replacement therapy. Concomitantly, the wound is prepared for grafting by daily or

twice daily dressings. By intensive treatment, grafting can usually be done within a week. Wound closure and subsequent treatment are the same as in other cases.

Acute contagious diseases of childhood are the principal complications, and upper respiratory infections are particularly troublesome because of added morbidity and risk of anesthesia, which may interfere with wound closure. Contractures at flexion creases can be minimized if wounds are closed early and if grafts are so placed as to produce scars parallel to the crease. Early motion helps keep joints mobile. Secondary plastic procedures can be used to correct residual scars that interfere with motion.

---

## ANTIBIOTICS

Clinical Use of Depolymerases of Streptodornase is reported by Joseph M. Miller, Milton Ginsberg, John A. Surmonte, Frank B. Ablondi and John H. Mowat.<sup>6</sup> Depolymerases of streptodornase may be administered in solution or suspended in lubafax® (surgical lubricant). Contents of each vial containing 100,000 units of activity are usually dissolved in 10-20 ml physiologic saline, amount of diluent depending on concentration of enzyme desired. A more dilute solution was used for treatment of a large burn (200,000 units in 1,000 ml saline). Generally, for treatment of localized collections of pus, stronger concentrations are desired. To facilitate application to a flat external surface 100,000 units may be suspended in 30 ml lubafax®. Solutions should be made fresh daily and stored in a refrigerator when not in use. Suspension in lubafax® keeps its potency for several days and should also be stored in a refrigerator.

Depolymerases of streptodornase are given for local effect only. Allergic reactions to the enzymes were not observed, but because they are antigenic, administration should be associated with the usual precautions. Principles guiding use of depolymerases are essentially those of varidase® or streptodornase.

Depolymerases will not cause lysis of fibrin and so should not be used when removal of a sterile collection of blood



is desired Slough and foreign bodies must be removed from the wound Blood supply must be adequate to provide magnesium ion to activate the enzymes, which must be applied in excess Proper pH must be maintained Depolymerases of streptodornase must be placed in direct contact with pus Products of digestion must be removed effectively and frequently to prevent reversal of reaction, permit more effective action of chemotherapeutic or antibiotic agents and provide more favorable conditions for healing Treatment of severe infections should be continuous

Of 20 patients treated, 15 had abscesses of various types, 3 had tuberculosis and 1 each, severe burn and pneumonia Excellent results were obtained in 17 and good response in 3 For the patient with pneumonia, depolymerases of streptodornase were put in a solution and used as an aerosol

Use of streptodornase alone substantiates earlier work in which varidase,<sup>6</sup> a combination of streptokinase and streptodornase, was used Infected wounds usually contain fibrin, and it is advantageous to have the streptokinase present with the streptodornase

**Neomycin-Nystatin for Preoperative Preparation of Colon** Isidore Cohn, Jr., and Alfred B Longacre<sup>7</sup> (Louisiana State Univ) used the following regimen for preparation of five patients having colon surgery low residue diet, a cathartic the first day of the program, daily enemas and neomycin-nystatin, 2 tablets every hour for 4 hours and then 2 tablets every 4 hours for 72 hours Each tablet contained 0.5 Gm neomycin sulfate and 125,000 units of nystatin Quantitative stool cultures revealed that after three days of therapy the stool was almost free from bacteria Side reactions were minimal

Neomycin-nystatin in combination with mechanical cleansing is one of the most effective means for preparation of the colon before elective surgery

**Preoperative Preparation of Bowel with Neomycin** was assessed by B C Rowlands and Eileen M C Scorer<sup>8</sup> (Sheffield Royal Infirmary), and optimal dose of neomycin for suppressing fecal pathogens of surgical importance was determined Neomycin was given orally to 35 patients, 14 received 1 Gm every 4 hours for 24 hours preceding opera-

(7) *Am Surgeon* 22 301 307 March 1956

(8) *Lancet* 2 950 952 Nov 5 1955

tion and 21 took 1 Gm hourly for four doses, followed by 1 Gm every 4 hours for the remainder of 24 hours. Complete sterilization of the bowel was achieved in 29% of the first group and in 45% of the second. No neomycin-resistant organisms developed. There was no difference in clinical results obtained with the two methods of administration. None of the operations was fatal, and there was no intraperitoneal infection or sepsis in abdominal incisions. In abdominoperineal resection, perineal wounds healed satisfactorily. No systemic reaction to neomycin, no intolerance and no toxic side effects appeared.

The main advantage of neomycin, in comparison with other preoperative drug therapy, is that the bowel apparently can be prepared safely for surgery within 24 hours. As with other forms of preoperative bowel sterilization, intestinal obstruction diminishes the effect of the drug. Presumed sterility of the bowel lumen should in no way excuse any deviation from exact and carefully performed technical procedures which are the basis of successful intestinal surgery.

---

## NEOPLASMS

**Some Observations on Epidemiology of Cancer in the United States** John R. Heller, Sidney J. Cutler and William M. Haenszel<sup>9</sup> (U.S.P.H.S.) carried out cancer morbidity surveys in 10 metropolitan areas of the United States in 1937 and again in 1947, including about 10% of the total population of the United States.

In 1947, out of every 100,000 residents, 430 had cancer at some time during the year. Compared with 1937, prevalence rate was 26% higher, incidence rate 30% higher and mortality rate 19% higher. In 1947, the age adjusted incidence rate for males was 331/100,000 and for females 330/100,000. In contrast, deaths due to cancer occurred at a rate of 169/100,000 among males and 147/100,000 among females, the difference being due to the inaccessible sites and poor prognosis of a larger proportion of cancers in males, e.g., stomach and lung cancer. Reported illness from cancer was

substantially lower among nonwhite persons than among whites. In 1947, cancer was diagnosed at a rate of 272/100,000 among nonwhites, compared with a rate of 333 for whites, the low incidence of skin cancer among nonwhites largely accounting for the difference. When skin cancers are excluded, it becomes apparent that cancer is being diagnosed at about the same rate in white and nonwhite females. The rate for nonwhite males is 14% lower, probably because the diagnosis is often missed.

Cancer rates increase rapidly during adult life and old age. Incidence rate is about 40/100,000 at age 25, 475/100,000 at 50 and 1 900/100,000 at 75. Among children under 10, the incidence is somewhat greater in boys than in girls. From age 20 to about 60, incidence is higher among women. Between ages 25 and 45, the rate in women is about twice that in men because of the high incidence of cancer of the genital organs and breast among the former. From about 60 on, incidence rate for men is higher, the difference increasing with age.

More than 500,000 new cases of cancer are being diagnosed in the United States each year, this number will increase to more than 750,000 by 1975. Of every 100 newborn children, 32 will have cancer at some time during their lives. Among persons surviving to age 65, 26 in 100 may be expected to have cancer during their remaining years. Cancer will occur in 31% of newborn white males during their lifetime compared with 36% of newborn white females, the difference being due primarily to the fact that white women can expect to live an average of 72.4 years compared with 66.6 for white men.

In men the risk of cancer of the digestive system is dominant with a lifetime probability at birth of 10.3 in 100. In women, the probability of cancer developing by age 65 is highest for the genital organs and breast. The probable number in whom cancer of the digestive system will develop from age 65 on is 9.9/100 men and 8.4/100 women. The probable incidence of leukemia during childhood (by age 15) is less than 1 in 1 000 for both sexes.

In females nearly one half of all cancers originate in the reproductive organs and nearly one fourth in the digestive system. Among males only one cancer in eight originates in the reproductive system while one third originate

in the digestive system. Cancer of the lung and bronchus occurs  $4\frac{1}{2}$  times as frequently in males, and the incidence of laryngeal cancer is 12 times as high. The greater frequency of nearly all forms of cancer except that of the reproductive organs in males may largely be due to exogenous factors.

Negroes have a higher incidence of cancer of the prostate and penis than whites. Among females, there is a higher rate of genital cancer in Negroes than in whites.

The outstanding change between the two survey periods was the large reported increase in cancer of the lung and bronchus by 1947. Both incidence and mortality rates more than doubled in 10 years, perhaps partly because of improved case finding. At least part of the reported increase in lung cancer incidence and mortality is real. There was a 24% decrease in incidence of stomach cancer, a 7% increase in hospitalization rate and an 18% increase in microscopic confirmation of diagnoses.

Early diagnosis of cancer is considered most conducive to successful treatment. Of every 100 persons in whom a diagnosis of localized cancer was made, 43 lived for at least five years after diagnosis, whereas of every 100 with diagnosis made after other organs had been invaded, only 3 survived five years. Only one half of all cases of cancer are being diagnosed while localized at the site of origin. This record should be improved since half of all cancers develop in organs accessible to direct examination by the physician in his office.

► [It is disappointing to learn that only 50% of cases of cancer are being diagnosed while localized at the site of origin. Can this be improved very much? When some cancers ordinarily produce no symptoms until far advanced, as for example in the esophagus, the stomach and the lung, are they likely to be diagnosed early? Perhaps someday a blood test for the presence of a cancer, as successful as that for syphilis, will be discovered. In a person with a positive test, a careful search could be made to locate the site of the cancer. At present the yield from repeated mass examinations of the population seems too small to be very practical. Some new technic like a blood test is urgently needed. An examination of the bone marrow, as described in the abstract immediately following, might be of some help, or the Schultz-Dale test described by Makari in the second abstract after this one may prove to be helpful.—Ed.]

Cancer Diagnosis by Bone Marrow Smears is discussed by C. H. Jarnet and H. E. Amy<sup>1</sup> (McMaster Univ.) on the basis of a study of 4,100 marrow aspirates. Of these, 55.3%

(1) Ann Int Med 44:617-629, April 1956

were positive for carcinoma, an additional 4.5% interpreted as positive were not confirmed clinically, 28.3% were negative for carcinoma but diagnostic of other conditions, and 6.8% were negative, but carcinoma was later revealed by biopsy. Marrow studies on 128 patients at admission (before other diagnostic studies) revealed four previously undiagnosed cases of pernicious anemia, one lymphosarcoma and four unsuspected carcinomas.

Tumor cells in marrow aspirates usually occur as large cell or small cell types, consistent in general cytology in a given case. The tendency of tumor cells to form "cell balls" or metastatic clumps differentiates them from loosely arranged cells of normal hemopoietic bone marrow. Their nuclei appear vesiculated, and the cytoplasm may be scanty or may occur as a homogeneous matrix for a large cluster of nuclei, with mitotic forms. The nuclei may also vary in affinity for stains, the chromatin network may be different and the cytoplasm may not show any evident variation. Denuded nuclei may be present, nucleoli are almost always found in some cell groups. The general site of origin of the tumor may often be suspected by size, arrangement and staining properties of cells.

The outstanding secondary cell pattern found in patients with metastatic tumors (also with other diseases) consists of an elevated plasma cell count, with increased eosinophils (without a comparable number of eosinophils in the peripheral blood), increased activity of lymphocytopoiesis and occasional fibroblasts. The elevated plasma cell count demonstrated a relation between a marrow stimulus to produce plasma cells and the level of plasma globulin in the marrow in conjunction with an increased sedimentation rate of the blood. This reaction was most prevalent in rheumatoid arthritis, ileitis and many cases of unexplained fever as well as in 85% of cancer cases. It is suggested that the plasma cell response in tissue to a specific stimulator (carcinogen etc.) may be comparable to the specific antibody response to certain bacterial invaders.

Repeated marrow examinations begun two years ago were made of 70 consecutive patients with breast carcinoma, who were treated without regard to marrow findings. The marrow cell patterns were graded into four groups: (1) definite micrometastases, (2) questionable single cells, mod-

erate myelofibrosis and secondary cell pattern, (3) secondary cell pattern only, (4) negative marrow. Two years later, 9 of the 15 patients in group 1 had died, 9 of 25 in group 2 returned with metastases. Only one patient in group 3 died, from causes unrelated to cancer, and none in group 4 showed recurrence.

The action of various chemical agents on malignant cell patterns of bone marrow was studied in multiple myeloma and lymphosarcoma cases. Radioactive phosphorus affects chiefly the desoxyribonucleoproteins, interfering with the synthesis assembly of nuclear constituents. In bone marrow, desoxyribonucleic acid takes up an appreciable fraction of labeled phosphate. A rapidly growing tumor, such as myeloma, with high mitotic index, can be retarded by  $P^{32}$ , which has a more pronounced effect on tumor growth than on normal hemopoietic tissue. The latter begins to regenerate in two to three weeks. With  $P^{32}$ , tumor destruction is greater and damage to hemopoietic tissue less than with chemical poisons, such as stilbamidine, urethane and nitrogen mustards.

Use of Schultz-Dale Test for Detection of Specific Antigen in Serums of Patients with Carcinoma is described with preliminary results, by Jack G. Makari<sup>2</sup> (Univ. of Texas). Schultz (1910) and Dale (1913) found that when sensitized guinea pig intestine or uterus is removed from the body and suspended in oxygenated Ringer's solution, maximal contraction will occur on exposure to even small amounts of antigen. Makari previously used this reaction to detect rickettsial antigen in egg yolk and cotton rat liver and also a soluble antigen in serums of patients with infective hepatitis and homologous serum jaundice. With the same method, he found a soluble carcinoma antigen in serums of carcinoma patients.

Actively or passively sensitized uterine horns of guinea pigs were used in the present studies and preliminary tests were made to determine optimal conditions for use of the method as a diagnostic test. Best specificity and sensitivity were demonstrated when serum or plasma was used fresh or after storage at  $-40^{\circ}\text{C}$ , or when platelet-intact or platelet-free plasma was used and the sensitizing antigen was of small particle size.

(2) Brit. M. J. 2 1291 1295 Nov. 26 1955

errors were at fault, due to frozen sections in eight and to paraffin sections in two. This low proportion of error in frozen section diagnoses (usually reported as about 10%) probably derived from the fact that the material examined was obtained from a limited region, and hence diagnostic possibilities were more circumscribed. Another factor may be greater technical facility, since several frozen section microscopies are performed daily, and all pathologists participate in examining them.

Most diagnostic difficulties are encountered in distinguishing between chronic interstitial pneumonia with epithelial proliferation and pulmonary carcinoma. In bronchial stumps and lymph nodes, it is difficult to diagnose invasion by anaplastic carcinoma, which may be confused with chronic nonspecific inflammation with fibroblastic proliferation. In such instances, a supplementary section stained by the van Gieson-Hansen method may be helpful.

The aims of frozen section microscopy during operation are diagnosis of clinically doubtful cases and trying to decide whether the lesion has been removed with a margin of healthy tissue. The pathologist's task is primarily to decide whether a lesion is neoplastic or inflammatory and within these groups malignant or benign, specific or non-specific. Particular morphologic details are less important, and there is no time for them. The pathologist should help the surgeon decide whether a lesion is operable, and if so in case of malignancy, whether sufficient tissue has been removed. Frozen section diagnoses are also valuable in surgical treatment of tuberculosis e.g. frequency of bronchial fistulas apparently has diminished since it has been possible to ascertain that the bronchial stumps are closed in healthy tissue.

Diagnostic accuracy presupposes that frozen sections are examined every day and by at least two pathologists.

**Simulation of Cancer by Oil Granulomas of Therapeutic Origin.** W. St. C. Symmers<sup>7</sup> (Charing Cross Hosp. London) reports 6 cases chosen from 14 similar examples seen during the past 10 years referred from different parts of Britain and abroad. Each patient presented a tumor-like oil granuloma which was mistaken for cancer. In each the lesion was due to introduction of an oily substance into the tissues.

during treatment of an earlier disease. In three, possible diagnostic significance of this therapeutic history was not appreciated until after microscopy had shown the real nature of the granuloma. In the other three, history of the previous illness had not been elicited.

Due to incorrect clinical diagnosis of cancer, four patients received unnecessarily radical treatment. Abdominoperineal excision of the rectum was performed in two, for an anal oleogranuloma following injections for hemorrhoids and for an ischiorectal oleogranuloma after packing of an abscess cavity with paraffinized gauze. A radical mastectomy was performed in the third for an oleogranuloma following packing of a breast abscess cavity with medicated paraffin paste. In the fourth, bilateral orchiectomy was done for a scrotal oleogranuloma following injection of a hydrocele sac with niaoul oil in liquid paraffin.

One patient in whom radical surgery was avoided by histologic demonstration of the true nature of the lesion had an intramuscular oleogranuloma simulating sarcoma following injections of an oily suspension of bismuth for syphilis. In the other, there was simulation of sarcoma by an intramuscular pseudotuberculous oleogranuloma following injections of penicillin with beeswax in oil for recurrent furunculosis.

Radical treatment would probably have been avoided in all the patients had possibility of a granuloma been considered and biopsy performed. A common feature was failure to elicit history of previous treatment with oily substances or, when it was known, to recognize its significance.

► [This article, of course, is apparently considered with the three previous articles. If frozen section biopsies had been made, mutilating operations would have been avoided in some of the patients—Ed.]

**Multiple Primary Malignancies: Case Report of Four in Succession** is presented by Walter G. Maddock, John J. Lipinski, Robert C. Lien and Howard L. Alt<sup>8</sup> (Northwestern Univ.).

A housewife, 64, had always taken care of her health and had had excellent medical care. In November 1927, at age 38, radical mastectomy was performed for undifferentiated cell carcinoma of comedo type. No metastases were identified in regional lymph nodes. In March 1940 (age 51), hysterectomy with bilateral salpingectomy and oophorectomy was done for papillary cystadenoma of the right ovary with malignant degeneration. In July 1947, at age 58, resection

(8) A M A Arch Surg 72 628 633, April, 1956



of distal two thirds of sigmoid and upper rectum with end to end anastomosis was carried out for adenocarcinoma, grade 2. No metastases were found in sigmoid mesenteric or periaortic lymph nodes. There was no evidence of carcinoma in the liver or pelvis from this tumor or previous ovarian malignancy. In May 1948, at age 59, a left radical mastectomy was performed for adenocarcinoma, grade 3, duct cell type. No metastases to regional lymph nodes were identified. In May 1949, a laparotomy was done for intestinal obstruction due to adhesions, and no abdominal carcinoma was evident. In the spring of 1954, the patient was well but by midsummer showed signs of pulmonary and liver metastases. At autopsy, lungs, liver and retroperitoneal lymph nodes were extensively infiltrated with duct cell sclerosing carcinoma similar to that of the fourth malignancy from the breast. Thirteen years elapsed between the first and second malignant growths, the last two were in rapid succession. With 21 years between the two breast tumors, there is no doubt that the second was another primary growth. It also was of a different histologic type from the 1927 lesion.

Four other cases of four primary successive malignancies were collected from the literature. All patients were women, all had a cancer of the colon or rectum, four of the five (including the present case) had a cancer of female reproductive organs, four also had a breast cancer and two had bilateral primary breast lesions.

The frequency of multiple malignancies should alert every physician confronted with one tumor to look for a second cancer, both at the original examination and at subsequent check ups. In follow-up, examination of the site of the original tumor and its common routes of extension is not enough. Every six months an interval history should be taken, with particular questioning on common symptoms of cancer and a complete physical examination and laboratory study, especially covering common sites of cancer.

► [This striking case makes one wonder about the pathogenesis and indeed raises the question why are not similar cases of multiple malignancy seen more often? Obviously this woman must have had a low resistance to the carcinogenic factors responsible for the malignant growths, but the question that naturally arises is why does not bilateral simultaneous cancer occur more often in paired organs? If for example in a carcinoma of the breast we assume that a blood borne carcinogenic factor of some sort has been responsible why have not both breasts responded to it in the same way much more frequently than one sees bilateral carcinoma of the breast occurring simultaneously?—Ed.]

**Heterologous Growth of Human Tumors and Normal Tissues in Subcutaneous Sites** is described by Helene Wallace Toolan<sup>9</sup> (Sloan-Kettering Inst.) With progressive develop

ment of x-ray techniques and/or the event of cortisone, human tumors transplantable in subcutaneous tissues of the rat and hamster are available in such large quantities that one tumor alone produces a harvest of 1-2 kg/week though the original specimen from the patient weighed less than  $\frac{1}{2}$  Gm, 5-10 Gm is obtained from each rat. Human tumors, carried in animals, have been transplanted easily to tissue culture and established as permanent in vitro strains, they have been implanted on chorionallantoic membrane and in the yolk sac of the chick and have not only proliferated there but, in the case of one bone tumor, produced widespread metastases in subsequently hatched chicks. This same tumor regularly metastasizes in its animal hosts within the short period (two weeks) after implantation that they remain alive. The neoplasms have remained human in their morphology, their antigenic nature and their chromosome make up even though two of them have been transplanted for over three years.

No correlation has been found between growth rate or metastases of the tumor in the human donor and the "take" or rapidity of proliferation in the animal host. Different specimens, obtained at various times from the same donor, may vary in transplantability, with the metastatic or last-taken biopsy not necessarily the most proliferative. Degree of sterility and relative freshness of material are more important than the stage of the patient's disease. One transplantable soft part sarcoma was removed three years ago from a patient who is alive and entirely well. The tumor had grown very slowly for six months before excision yet it produces an increment of over 100 fold in two weeks when implanted in animals and invariably causes death. This may indicate that many patients have resistance to their own neoplasm. Human tumors that do not grow, or proliferate poorly in animals, as contrasted with their behavior in patients, may need growth stimulating factors not supplied by animal hosts. Growth never occurs in untreated control animals. The avian egg however, needs no conditioning.

Under comparable circumstances not all human tumors grew equally well. Epidermoid carcinomas were most likely to survive and proliferate even autopsy material 8-10 hours post mortem would sometimes grow. Bowel tumors con-

versely, had to be put into the host animal within minutes after removal. Mammary adenocarcinomas, especially those with large amounts of stroma, and brain tumors were also difficult to propagate in animals. Approximately 3% of neoplasms screened reproduce themselves 80 to 100-fold in two weeks in conditioned animals. Other human cancers can be maintained in animal hosts but proliferate so slowly that the animals must be constantly treated with cortisone to procure noticeable tumor increment.

► [This fascinating achievement opens the way for a study of human tumors in many new ways. By this technic any amounts of a single human tumor can be obtained for study.—Ed]

**Environmental Causes of Cancer in Man** are discussed by Ernest L. Wynder<sup>1</sup> (Memorial Hosp., New York). Agents suspected of causing lung cancer are tobacco, chromate, radioactive dust, arsenic, lubricating oils, isopropyl oils, metal dust and fumes, paint, wood dust, nickel and asbestos. Those suspected of causing cancer of the larynx include tobacco and alcohol. Of the penis, smegma or other agents under the foreskin of the penis, of the bladder, beta-naphthylamine, bilharziasis and benzidine, of the oral cavity, tobacco, syphilis (tongue) and dietary deficiencies of the liver, dietary deficiencies, and of the skin and lip, ultra violet light, arsenic, tars, oils (mineral shale and paraffin), roentgen rays, tobacco (pipe lip), anthracene, asphalt and pitch.

Tobacco type cancers alone, involving the lung, oral cavity, larynx and esophagus, cause a large proportion of cancer deaths, at least in males. If to these are added cancers that seem related to smegma, nutritional deficiencies, radiation and various industrial agents, a large proportion of all cancers occurring in man are included. Further research may show other environmental causes as yet unsuspected.

Both prospective and retrospective epidemiologic studies show the risk of lung cancer to be considerably greater in smokers than in nonsmokers. This risk is increased with the amount of tobacco consumed (Fig. 8). Tobacco smoking is now regarded of causative significance in lung cancer for a variety of reasons. (1) Lung cancer has increased sharply in countries in which there has been a great increase in tobacco consumption, particularly of cigarettes. Notably low

(1) *M. Clin. North America* 40:629-645, May, 1956.

rates, as in Iceland, where tobacco consumption is low, re-emphasize this point. (2) The predominant male ratio is compatible with long term smoking habits of both sexes. (3) The gradual increase in smoking by women, beginning 20 years ago, is compatible with a slight increase in incidence of lung cancer among females. (4) The higher rate among urban as compared with rural population is compatible with greater cigaret consumption among city dwellers. (5) The characteristic peak among males in their late fifties and early sixties is compatible with the first major

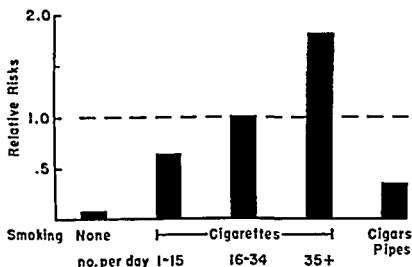


Fig. 8—Estimated relative risks of lung cancer patients compared to control groups for different smoking categories. (Courtesy of Wynder, E. L.: *M. Clin. North America* 40:629-645, May, 1956).

upswing in cigaret consumption some 30-35 years ago. (6) Considering the latent period of cancer, the increase of lung cancer is compatible with the increase in sale of cigarets. (7) Epidermoid cancer is but rarely found in areas not exposed to specific extrinsic irritation. Recently precancerous changes were demonstrated in the sectioned bronchi of heavy smokers. (8) Statistical tobacco data are regarded as significant by many clinicians who have seen many lung cancer patients. (9) Condensed cigaret smoke has induced epidermoid cancer of the skin in several strains of mice.

It is estimated that between 80 and 90% of all squamous and anaplastic lung cancers occurring in man today would not occur in the absence of smoking. Since lung cancer represents the commonest cause of cancer deaths among males

in many western countries, the preventive measures required are of foremost importance.

**Experimental Production of Carcinoma with Cigaret Tar:**  
**II. Tests with Different Mouse Strains.** Ernest L. Wynder, Evarts A. Graham and Adele B. Croninger<sup>2</sup> (Washington Univ.) have previously shown that skin cancer developed in CAF<sub>1</sub> mice painted with condensed cigaret tar obtained by the smoking of cigarets in a machine to simulate human smoking. In the present experiment, Swiss and C57 mice



Fig 9 —Carcinoma in Swiss mouse after 591 days (Courtesy of Wynder, E L., *et al* Cancer Res 15 445-448, August, 1955)

were painted with condensed cigaret smoke tar, about 40 mg., three times a week

Among 86 Swiss mice, 22 papillomas and 12 carcinomas were found (Fig. 9) after 24 months. The results for 89 C57 mice were 10 papillomas and 2 carcinomas. Application of croton oil, in addition to cigaret tar, appeared to accelerate the formation of lesions in both Swiss and C57 mice. The tar used differed from that in the first experiment in that it had been stored in acetone for a longer time.

Although the study demonstrated that cigaret tar can induce papillomas and cancers of the skin in strains of mice other than the CAF<sub>1</sub> strain, the two experiments are not comparable because they were done at different times and with differently stored tar. Results obtained by different investigators cannot be compared because of the variety of technics used in application of tar to the skin. It is suggested that condensed cigaret tar used in experiments be stored

(2) Cancer Res 15 445-448, August, 1955

refrigerated in undiluted form, in brown bottles, and that the solutions be prepared at biweekly intervals.

There is enough clinical, statistical and incidence data to prove a causative relation between cigaret smoking and lung cancer in man. The purpose of laboratory studies in animals is to identify active carcinogenic components that must be in cigaret tar. It is assumed that the carcinogen(s) isolated for the animal will be the carcinogen active for man.

**Cancer in Adults Before Midlife.**<sup>3</sup> Each year more than 20,000 deaths from cancer occur in the United States in patients aged 15-44, representing one fourth of the total

TABLE 1.—MORTALITY FROM MALIGNANT NEOPLASMS AMONG WHITE PERSONS, AGES 15-44 INDUSTRIAL POLICYHOLDERS, METROPOLITAN LIFE INSURANCE COMPANY, 1953-54†

SITE	AGES 15-24		AGES 25-34		AGES 35-44	
	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES
AVERAGE ANNUAL DEATH RATE PER 100,000						
Malignant neoplasms—Total	84	64	174	183	488	674
Digestive organs and peritoneum	.5	6	29	29	134	130
Respiratory tract	.2	1	1.5	6	11.1	2.3
Breast	—	*	1	3.2	.2	19.4
Genital organs	1.1	.8	1.8	4.2	10	18.1
Brain and nervous system	9	.8	20	10	43	2.6
Bone	.5	4	4	.5	.2	4
Lymphatic and blood forming tissues	4.2	30	6.5	44	7.2	5.2
Hodgkin's disease	1.3	10	24	17	20	1.3
Leukemia	19	1.5	2.5	1.8	2.6	24
Other, including lymphosarcoma	10	.5	16	9	2.6	1.5
PERCENT OF TOTAL						
Malignant neoplasms—Total	100.0	100.0	100.0	100.0	100.0	100.0
Digestive organs and peritoneum	5.8	8.7	16.7	16.6	27.5	19.3
Respiratory tract	2.7	2.2	8.7	3.3	22.8	3.4
Breast	—	.5	.3	17.7	.5	28.8
Genital organs	12.9	13.0	10.4	22.7	2.0	26.8
Brain and nervous system	11.2	12.5	11.8	5.6	8.8	3.8
Bone	5.8	7.1	24	10	.9	6
Lymphatic and blood forming tissues	50.0	46.8	37.1	24.1	14.8	7.8
Hodgkin's disease	15.2	15.8	13.9	9.1	4.2	2.0
Leukemia	22.3	22.8	14.2	10.0	5.2	3.5
Other, including lymphosarcoma	12.5	8.2	9.0	5.0	5.4	2.3

\*Less than 0.05

†Data for 1954 are provisional

(3) Statist Bull Metrop Life Insur Co. 36 1-4, June, 1955

mortality from disease at these ages and about one-twelfth of all deaths from cancer. There are about 65,000 new cases of cancer yearly in this age group. In males the incidence is 25.3/100,000 at ages 15-24, 47.2/100,000 at ages 25-34 and 127.9/100,000 at ages 35-44. In females the rate is 26.8/100,000 at ages 15-24, 85.9/100,000 at ages 25-34 and 256.3/100,000 at ages 35-44. At ages 15-24, virtually half of all cancer deaths in each sex are from malignancies of the lymphatic and blood-forming tissues (Table 1). From ages 25-34, cancer of the breast and genital organs accounts for two fifths of the total female mortality from cancer. The

TABLE 2—AVERAGE ANNUAL DEATH RATES PER 100,000 FROM MALIGNANT NEOPLASMS IN WHITE PERSONS, AGES 15-44 INDUSTRIAL POLICY HOLDERS, METROPOLITAN LIFE INSURANCE COMPANY, 1953-54 AND 1943-44†

AGE PERIOD (YEARS)	MALES			FEMALES		
	1953-1954	1943-1944	PERCENT CHANGE	1953-1954	1943-1944	PERCENT CHANGE
15-24	8.4	9.6	-13	6.4	7.4	-14
25-34	17.4	14.9	+17	18.3	20.0	-9
35-44	43.8	49.6	-2	67.4	82.4	-18

†Rates for 1954 are provisional

digestive organs account for one sixth of all cancers in both sexes at ages 25-34. Among men, cancers of the brain and nervous system and of the genital organs comprise a significant portion of the total in this group.

At ages 35-44, cancer of the breast and of the genital organs accounts for 55% of all cancer deaths among women and cancer of the digestive system causes well over one fourth of the deaths among men. Almost as high is the death rate from cancer of the respiratory tract, which is five times as common in males as in females.

Among white females, the death rate from malignant neoplasms decreased between 1943 and 1944 and 1953 and 1954 in the age range 15-44 (Table 2). Among white males cancer mortality improved appreciably at ages 15-24 and was virtually unchanged at ages 35-44, in the group 25-34,

however, the trend was upward. The relatively favorable trend for women is accounted for partly by the considerable decline in the mortality from cancer of the genital organs. Malignancies of the digestive system also showed a downward trend in mortality among females, decreasing by about one third throughout the age range 15-44. The death rate from breast cancer, however, increased slightly. Among males, only cancer of the digestive system showed a decrease in mortality in each age group.

To some extent, the progress made in control of cancer among adults before midlife reflects both increased tendency to seek medical care earlier in the course of the disease and advances in methods of diagnosis and treatment. Many lives could be saved if more cancers were detected early and treated promptly.

**Antiemetic Effect of Chlorpromazine (Thorazine®) in Cancer Patients** is reported by Sidney Fink and William Allen Winslow<sup>4</sup> (Montefiore Hosp., N. Y.). Fourteen patients had advanced neoplasm and one Kimmelstiel-Wilson's disease. All had intractable nausea and 12 frequent vomiting, which were considered due to radiation therapy in 6, partial intestinal obstruction in 4, uremia in 3, gastroduodenal fistula in 1 and cholemia in 1. Eight had received one or more standard antiemetic drugs, with little effect. Most patients showed stigmas of advanced disease, with pallor, weakness and malnutrition. Several were in terminal stages and were receiving only supportive care.

Initially, 25 mg chlorpromazine was given every four hours, orally whenever tolerated. If the intramuscular route was necessary, it was usually possible to change to oral medication after two or three injections. Dosage in some patients was raised to a maximum of 50 mg every six hours.

Nausea was markedly relieved or completely eliminated in 12 patients. 2 showed fair improvement and 1 had only mild nausea. Frequency of vomiting greatly decreased in 10, 4 showed slight or fair effects and 1 showed no effect, the last 5 all had partial gastrointestinal tract obstruction. The effect of chlorpromazine was compared with that of other medication or of placebos in 11 patients. Nausea or vomiting recurred during placebo trials in 10. Dramamine,<sup>®</sup>

(4) *Gastroenterology* 28:731-735 May 1955



given to four patients, afforded some relief and was more effective than placebos but not so effective as chlorpromazine

Drowsiness, found in 3 of 15 patients appeared at dosage levels averaging 150 mg daily. In all three, it became minimal on lower dosages, with retention of antiemetic and anti-nausea effects. Xerostomia was noted in two patients. No other clinical ill effects were detected. Laboratory tests revealed no effects that could be attributed to chlorpromazine. The minimal side effects did not necessitate interruption of therapy.

Relief of Pain in Cancer Patients is discussed by Danely P. Slaughter, Harry W. Southwick (Univ. of Illinois) and Harold L. Harris<sup>5</sup> (St. Francis Hosp., Evanston, Ill.). Many patients with incurable cancer need control of pain. This can be achieved by treatment which eliminates the tumor or causes temporary regression or by treatment which obtunds perception of pain or eliminates specific pain pathways. Direct attack on the tumor is best but can be done in only a few patients and only early in the disease. Palliation by tumor control is based on the concept that all malignant tumors have fairly definite behavior patterns of growth and spread and that the uncontrolled natural history of a given tumor is predictable within reasonably broad limits. The ultimate goal in partial or palliative tumor control is to arrange a chemical death from hepatic, renal or pulmonary failure. Except for a few tumors, it is often possible to channel the inevitable progression of an incurable cancer in a manner that minimizes or, rarely, eliminates pain.

Surgical relief falls into two categories—relief from obstruction and amputation or adequate excision of painful or ulcerated tumor masses. Obstruction is usually amenable to surgical relief even if only palliative, in the following areas: airway, swallowing, gastric, small bowel, biliary tract, colon and urinary tract. Excisional surgery is almost always preferable to bypassing procedures. In patients with cancer obstructing the extrahepatic biliary tract, every effort should be made to shunt bile flow internally if the tumor is inoperable.

Sarcomas and melanomas of the extremities and occa-

sionally metastatic cancer, may become huge ulcerating tumor masses that produce a useless extremity and cause severe pain, which may become intolerable. Amputation may be used in such cases. Amputation is occasionally necessary in some inoperable breast cancers.

Curative use of radiotherapy is limited to surface lesions or intracavitary irradiation of cancer of the upper respiratory tract and uterus. Radiation is useful in some cases of lymphomas, metastatic mammary or papillary thyroid cancer and some ovarian cancers. Almost all malignant tumors are radiosensitive to some degree. Localized painful metastatic deposits of relatively radiosensitive cancers are very effectively treated by irradiation.

Though no curative chemotherapy has been achieved, effective palliation is now possible in several clinical situations. Nitrogen mustard is effective in temporarily controlling systemic and disseminated Hodgkin's disease, lymphosarcoma to a lesser extent and leukemias to a still lesser extent. It is useful in bronchogenic carcinoma and in some other cancers when it is injected directly into the arterial blood supply of the tumor area. Aminopterin, methopterin, triethylene melamine and triethylene phosphor amide are effective in some inoperable cancers. Radioactive iodine and phosphorus are useful in some cancers.

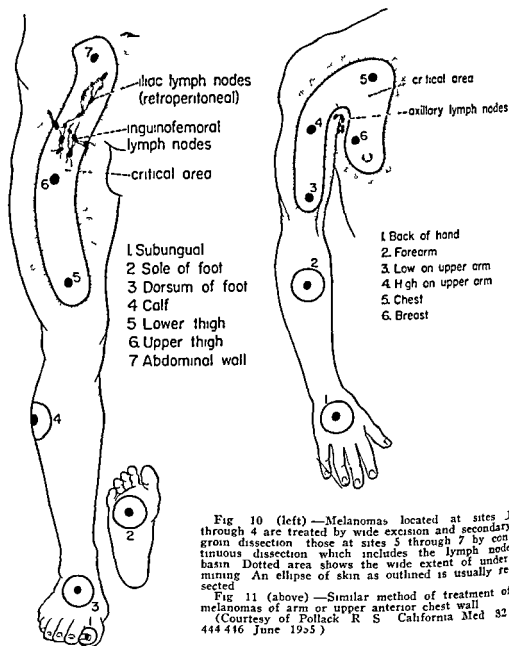
Castration or estrogen therapy, or both, is excellent palliation for prostatic cancer. Endocrine therapy is useful only for patients with advanced, disseminated and otherwise untreatable breast cancer. Castration, androgens and adrenalectomy are useful in patients under 55 with breast cancer. Patients, aged 55-65, with breast cancer are least likely to respond to endocrine management. Painful metastatic and recurrent breast cancer in patients over 65, when other treatment has failed, is most likely to regress on estrogenic therapy.

Neurosurgical operations are effective if performed before the pain pattern becomes fixed. Operations include peripheral nerve section, dorsal rhizotomy, chordotomy and lobotomy. Operative mortality is low.

Pharmacologic control of pain can be obtained with codeine, dilaudid,<sup>\*</sup> morphine or demerol.<sup>\*</sup> The likelihood of addiction is minimized if the dose of narcotic drugs gives relief from pain but does not induce narcotic sleep.

or euphoria Thorazine,<sup>®</sup> 10-15 mg three times daily is a useful adjunct to narcotic therapy

**Surgical Treatment of Melanoma**, recommended by Robert S Pollack<sup>6</sup> (Mount Zion Hosp, San Francisco), is wide



and deep excision and, where feasible, dissection in continuity with regional lymph nodes, often necessitating a skin graft to cover the defect When melanoma occurs in an area close to a lymph node group (neck, axilla or groin),

dissection including a wide block of tissue, deeply undermined, and adjacent lymph nodes is practical (Figs 10 and 11) If the primary tumor is on the sole of the foot, lower forearm or back, continuous dissection is not possible There is no advantage in waiting two weeks between removal of primary melanoma and secondary excision of lymph nodes, or of removing a narrow strip of skin between primary tumor and nodes, the length of an extremity, on the supposition that it contains involved intervening lymphatic pathways Occasionally melanoma may be situated in the midline of the back, abdomen or neck, or midway between axilla and groin, so that involvement of two lymph node groups is likely In such instances, watchful waiting, with delay of lymph node excision until metastasis is suspected, seems practical If metastasis to lymph nodes has already occurred, dissection of both groups in continuity with the primary lesion, if feasible, should be done

Regional node dissections put up a block or dam admittedly temporary, against rapid, widespread dissemination Recurrences often appear as intracutaneous or subcutaneous nodules proximal to the lymph node bed, and can be locally removed without too much change in prognosis certainly with better prognosis than if the first sign of recurrence were enlarged axillary or inguinal lymph nodes

Major amputations for melanomas of the extremities are not recommended since most cures are in the group in which local excision and regional node dissection will suffice Melanoma is not a certainly fatal disease, in one large series, five year survival, regardless of stage was 21% (14% for patients with lymph node metastasis at operation and 40% for those without it)

Some melanomas arise from compound and junctional nevi In view of the frequency of melanoma and the infrequency of moles or nevi on the soles of the feet and on external genital organs, moles in these areas should be removed routinely

Use of Nitrogen Mustard in Treatment of Serous Effusions of Neoplastic Origin Austin S Weisberger, Bennett Levine and John P Storaasli<sup>7</sup> (Univ Hosp, Cleveland) instilled nitrogen mustard directly into the effusion of 30 patients with pleural, 11 with peritoneal and 2 with peri-

cardial effusions Carcinoma of the breast was present in 12, ovarian carcinoma in 10, lymphomas in 6, bronchiogenic carcinoma in 3 and miscellaneous tumors in the others Patients with pleural and peritoneal effusions received nitrogen mustard in a single injection of 0.4 mg/kg, and the two with pericardial effusions received 10 and 22 mg, respectively Paracentesis was performed, and while there was still a free flow of fluid the nitrogen mustard was instilled with a small rubber catheter The patient's position was changed every 5-10 minutes for one hour to insure more uniform distribution of the material throughout the serous cavity The next day as much fluid as possible was removed at paracentesis

Significant improvement was seen in 28 patients In 20 there was no reaccumulation of fluid and in 8 there was marked reduction in the amount Of these 28, 20 were living at the time of the report, with improvement lasting 6-24 months in 10 patients and 2-5 months in the rest The best response was obtained in patients with carcinoma of the breast or ovaries Of those in whom the malignant effusion was completely eradicated, one was alive and well 24 months after therapy Three other patients had survived for longer than 12 months and were still asymptomatic Six had remained asymptomatic for periods of 6-10 months after therapy

Of 30 patients with pleural effusions 18 were improved and of 11 with malignant ascites, 8 were improved Both patients with pericardial effusions improved Side effects of the treatment were minimal, nausea and vomiting being less than after intravenous administration

The results compare favorably with those obtained with radioactive colloidal gold Nitrogen mustard is easier to use than the latter, more universally available and less expensive and presents no radiation hazard It may give better results when combined with radioactive colloidal gold

Relationship of Nucleic Acid Anabolism to Treatment of Cancer is discussed by C. P. Rhoads<sup>8</sup> (Sloan Kettering Inst.), with emphasis on the analogy between cancer and parasitic microorganisms Cancer cells of animal and human origin have now fulfilled all of Koch's postulates (1) demonstration of the invading cell in affected tissues (2)

cultivation outside the body, and (3) induction of the disease by cultivated organisms. The acquisition of resistance to therapeutic agents is now also as demonstrable for cancer cells as it is for invading bacteria. These facts justify a vigorous effort to find chemotherapeutic agents capable of selective destruction of cancer cells without intolerable injury to normal tissue.

Chemotherapy of cancer is based on the following principles:

1. Nucleic acid is the vulnerable point of the cancer cell, and its construction and turnover differ in normal and in neoplastic cells.

2. Nucleic acid in cells is in dynamic equilibrium and can be synthesized by dividing cells from simple precursors. However, since these precursors are universally employed in reproduction of all cells, specific destruction of any single cell type cannot be achieved by making any of them unavailable.

3. Demonstration of uptake of pre-formed precursors of nucleic acid has modified completely the chemotherapeutic approach to cancer control, making it a rational, rather than an empiric study.

4. Each species has its specific requirement for pre-formed precursors of nucleic acid, as does each cell type of the same species. This principle probably holds for neoplastic as well as for normal cells and should specifically set apart one from the other.

5. Different components of deoxyribonucleic acid (DNA) prepared from different tissues have been separated. This provides chemical substantiation of the metabolic data indicating that nucleic acid is not the same in different cells but differs for each type in constitution as well as, in requirements for replication.

6. The foregoing data pertaining to animal cells, have recently been shown to hold for man. Hamilton administered  $C^{14}$  labeled adenine to a patient with lymphatic leukemia and recovered it in the nucleic acid of the neoplastic cells, where it remained for almost a year. Clearly, either the life of the leukemic cell is unbelievably long or it employs, in duplication, large molecules related to nucleic acid passed down from its progenitors, i.e., from cell to cell. Since viruses are aggregates of nucleic acid molecules,

this observation (if confirmed) may tend to bring together the viral etiology and mutation induction of cancer

7 The demonstrable specific uptake of marked purines by certain mammalian cells, and not to similar extent by others, opened the possibility that modified purines might exert specifically injurious (antimetabolite) effects and selectively stop reproduction of cancer but not of normal cells. Since synthesis of nucleic acid from simple sources by dividing cells requires folic acid as catalyst, impairment of this catalytic activity by certain analogues (4-amino folics) in animals bearing certain transplantable neoplasms inhibits the growth of cancer for a time, but cure is not effected. To enhance the incomplete cancer-restraining ability of compounds exerting antifolic activity, blocking a second pathway by use of modified purines as antimetabolites was strongly indicated.

8 Simultaneous culture of normal and neoplastic cells of similar origin growing at the same rate, for definition of the selective destruction of one without that of the other, is a recent development.

9 Specific susceptibility of some animal and human cancer cells in vitro to certain antipurines has been demonstrated.

10 Acquired resistance of cancer cells to nucleic acid antimetabolites, e.g., antipurines (6 mercaptopurine and 8 azaguanine) has been demonstrated.

11 There is evidence however, that new sensitivity develops with acquired resistance. In one type of animal leukemia acquisition of resistance to an antifolic brings with it new sensitivity to an antipurine used in combination with azaserine. It is hoped that this will be found to obtain for a variety of resistant neoplastic cells.

12 The demonstrable existence of multiple pathways of nucleic acid metabolism in neoplastic as well as bacterial cells has led to combination chemotherapy. Unless there are more pathways of cell nucleic acid metabolism than there appear to be it should be possible to learn them all and to break every one. At present they are not all known.

Not long ago to dream of a pill for cancer was tantamount to insanity. Now there are several pills. Their effect is feeble and transient and only certain cancer patients respond but responses do occur. That several types of trans-

plantable cancer in animals can be wholly destroyed by systemic chemotherapy justifies continued work to extend the basic principles already developed, in the hope for further cancer control in man

► [I from personal observation on many occasions I can assure the readers of this abstract that the work of Rhoads and his colleagues at the Sloan Kettering Institute is most exciting. It would seem as if a cure for at least some cancers is just around the corner. At least it is nearer than ever before—Ed]

**Biophysical Effects of Ultrasonic Energy on Carcinoma and Their Possible Significance** are discussed by Justus F. Lehmann and Frank H. Krusen<sup>9</sup> (Mayo Clinic and Found.), who found that ultrasonic energy caused destructive phenomena of cavitation only sporadically in solid tumors. Occurrence of cavitation was largely inhibited by the high volume percentage of cells in the tissues.

To the authors it seems unlikely that the healing effect of ultrasonic energy can destroy cancerous growths without destruction of normal tissues. However, combined with x-ray therapy, ultrasonic treatment appears to increase the efficiency of the former. It is conceivable that this property of ultrasonic energy may be of practical value.

The fact that the effects of ultrasonic energy were not at all uniform because of the nonuniformity of the intensity in the sound field and the fact that the increase in efficiency of x-ray treatments was not a major one indicate the limitations of possible therapeutic application of ultrasonic energy in combination with x-ray irradiation. However, it is conceivable that these limiting factors can be improved by changing the experimental conditions.

There is no definite indication that ultrasonic energy will have a place in the therapy of cancer.

**Radioactive Gold Treatment Results in 85 Effusions Due to Cancer**, treated in Mt. Sinai Hospital, New York, since July 1, 1951, are reported by Norman Simon.<sup>1</sup> At first, patients were selected for treatment only if multiple taps were required, but recently gold was injected at the time of the first tap. Results in the latter are uncertain. Favorable results indicate complete suppression or definite decrease in fluid formation.

Among 46 patients with pleural effusion, results were

(9) Arch. Phys. Med. 36:452-459, July 1955.

(1) J. Mt. Sinai Hosp. 22:96-98, July-Aug. 1955.



favorable in 20 (43%). The commonest tumor producing pleural effusions was breast cancer, in which most gratifying results were obtained (13 of 20). Only two of eight patients with carcinoma of the lung were benefited; nevertheless it is worth while to attempt suppression of fluid with gold if fluid accounts for the major symptoms or if frequent taps are required. Only 2 of 10 patients with primary site of the cancer undetermined were benefited. Both patients with Hodgkin's disease responded favorably.

Beneficial effects were observed in 13 of 39 patients (33%) with ascites secondary to cancer. Of the more than half (22) with ovarian carcinoma 7 showed successful results. In the two patients with spillage of carcinomatous cysts, radioactive gold was injected postoperatively in an attempt to prevent seeding of free carcinoma cells. Results were uncertain. Three of eight patients with ascites with primary site of the cancer not definitely known were favorably influenced.

Of the total 85 patients, 33 (39%) were favorably influenced. Better statistical results could be obtained by giving gold only to patients with effusions due to slowly growing cancers of the breast or ovary, but occasional good results in other primary tumors justify less restricted use of the treatment.

---

## THE HEAD

**Developments in Rotary Abrasive Technics for Removing Acne Scars and Other Cosmetic Defects.** Joseph Eller<sup>2</sup> (City Hosp., New York) reports that he has used the Schreus high speed apparatus in hundreds of cases with most satisfactory cosmetic results. The Schreus apparatus consists of a flexible shaft, hand piece, protective sleeve, foot control, heatless stones of various sizes and motor. Heatless stones and diamond and ruby fraises used at 30,000 rpm give much smoother grinding, more satisfactory dermal abrasion and better cosmetic results than steel wire brushes driven at 12,000 rpm.

(2) New England J Med 253 11-14, July 7, 1955

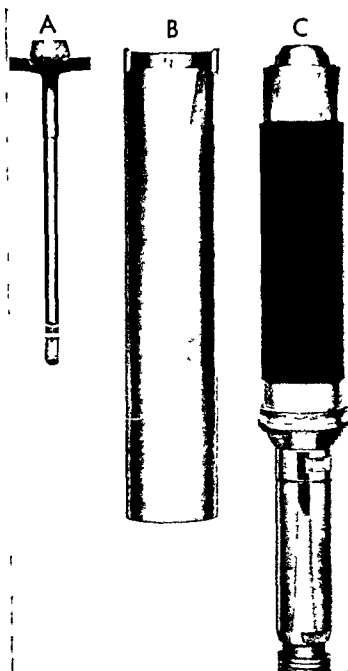


Fig 12—Heatless stone grinder and adapter (A), with protective sleeve (B), which fits over the handle and grinding stone to prevent spattering, and handle on flexible revolving shaft (C) (Courtesy of Eller, J J *New England J Med* 253 11-14, July 7, 1955)

Complete control of the rotary heatless stone grinder (Fig. 12) by the operator is necessary. With the thumb as a pivot, the skin is stretched taut, and with very light pressure the area is abraded, a thin layer at a time. The protective sleeve, which collects the ground tissues and blood and

prevents spattering gives the operator a clear working field

In most cases, procaine cobefrin® local anesthesia may be used, since with the higher velocity apparatus it is not necessary to harden the skin by freezing. With procaine anesthesia the field is always visible and not disguised as by freezing. In cases of dermal abrasion in which refrigeration anesthesia is desirable, freon mixture is preferable to ethyl



Fig. 13 — Male patient with acne scars of 18 years duration before abrasion treatment (Courtesy of Eller, J. J. *New England J. Med.* 253:1114, July 7, 1955)

chloride since it is nonexplosive and nontoxic. It is sprayed on in the same way as ethyl chloride.

For the average case of acne scars, one dermal abrasion done with the Schreus apparatus and stone grinders was sufficient for a satisfactory result (Figs. 13 and 14). For more severe and deeper pitted scars, second or even third dermal abrasions were necessary. These could be repeated at intervals of five to six months. The procedure can be carried out with ease in the operating room of the physician's office. The patient may go home after the operation and return daily for five or six days to have the dressings



Fig 14—Patient after single dermal abrasion by high speed heatless stone grinders using freon a noncombustible refrigerant as anesthetic. (Courtesy of Eller J J New England J Med 253 11 14 July 7 1955)

changed. Complete epithelization with no visible scar usually takes place within 14 days.

**Turban Tumors** L. J. Chalstrey<sup>3</sup> reports on a patient with many nodules on his scalp and body. Members of the family also had similar tumors.

Man 62 had multiple nodules on the head and body that first occurred at age 19. They ranged in size from 0.3 to 4 cm (Fig 15) and were of varied shape, some being flat and others nodular or cystic. The tumors on the scalp were excised and a split thickness graft applied. Histologic sections revealed basal cell carcinoma consisting of nodular formations covered by a thin flat intact epidermis. The scalp was then irradiated.

The patient stated that his mother, grandmother, son, daughter (Fig 16), brother and sister (Fig 17) had similar tumors.

Turban tumors usually have their onset during adolescence or early adult life and grow slowly at first and later more rapidly until by the sixth decade multiple masses are present on the head and often on the rest of the body.



Fig 15 Patent before operation (Courtesy of Chalstrey L J St Bartholomew's Hosp J 59 378 383 December 1955)



Fig 16 (left) Daughter of the patient  
Fig 17 (right) Sister of the patient  
(Courtesy of Chalstrey L J St Bartholomew's Hosp J 59 378 383 December 1955)

In most cases the head remains the main site of the disease. General health is unimpaired and the lesions are painless, the only complaint being their unsightliness. In advanced cases the large tumors are easily injured and heal with difficulty. Treatment is excision and skin grafting as necessary. Electrocautery can be used in some cases. Although the tumors are radiosensitive, x-ray therapy is not practical, since it may cause the lesions to regress but does not cure.

These tumors of the skin and its epidermal appendages seem to be the manifestations of a common, inherited, underlying pathologic process of unknown nature. They probably originate in both sweat glands and pilosebaceous glands, although some authorities favor one of these sites over the other.

► [The author states that a descriptive term might be applied to them, such as 'multiple benign familial nodular, subepidermal basal cell epithelioma with hyaline and cystic degeneration.' Obviously, this term is too long to be practical but yet it gives one an idea of the pathologic features. Fortunately, the condition is rare.—Ed.]

---

## THE NECK

**Modern Indications for Tracheotomy** Special Reference to Management of Cases Requiring Artificial Respiration. Alfred S. H. Walford<sup>4</sup> (Cambridge) discusses the problem. With swallowing dysfunction, secretions, drink, food, vomit or blood may pass into the trachea, causing pulmonary complications. This may happen in acute anterior poliomyelitis, other diseases of brain and central nervous system, head injuries, tetanus and injuries to neck, mouth, pharynx and larynx. By tracheotomy and insertion of a cuffed tube the trachea can be sealed off, insuring that only air, or oxygen and nitrogen, can enter, while a free airway is simultaneously maintained. If respiration is diminished or absent artificial respiration must be administered. Tracheotomy should be done only when postural drainage and suction have failed.

In the Copenhagen poliomyelitis epidemic of 1952, 250 of 316 severe respiratory cases were treated by tracheotomy. During the first month, when older methods of treatment

(4) Proc. Roy. Soc. Med. 48:947-951, November, 1955.

were used, 27 of 31 patients with respiratory and/or pharyngeal paralysis died (85-90%) Of the 250 treated with tracheotomy, insertion of a cuffed tube and positive respiration, 100 died (40%) Late in the series, mortality rate decreased to 23%, principally because of improved technic

The cuffed rubber tube can be removed as soon as the paralysis of swallowing is overcome and the patient can perform respiration If recovery of respiration is not nearly complete, a metal tracheotomy tube should be left in place until automatic respiration has become strong If these patients contract an acute upper respiratory infection, they may again require forced respiration

There are several advantages to maintenance of respiration by means of tracheotomy (1) It allows gases to enter and leave the lungs while preventing entry of fluids and solids from pharynx (2) Trachea and bronchi can be kept free from secretions by use of suction or forceps (3) It allows easy access to patient for lung examination and for all nursing and x-ray purposes (4) The patient can easily be moved and may even be ambulant (5) The patient is comfortable and usually not apprehensive There are also disadvantages (1) Patients may be saved who might be better dead, but this cannot be determined at the time, since some severe bulbar cases recover completely (2) The weaning period may be difficult (3) Trained personnel is essential (4) Stenosis of trachea may occur The Copenhagen figure was 3% stenosis

Tracheotomy is now often used in the treatment of severe tetanus, and when curare and heavy sedation are given, forced respiration may also be necessary

In tracheobronchitis of children, it is better to avoid tracheotomy, if possible, by using antibiotics, moistening of inspired air and use of oxygen and detergents to soften secretions Once tracheotomy has been done, the child loses propulsive cough, and frequent removal of the crusts is often required

## THE THYROID

**Thyroid Carcinoma in Children** is rare, though it is being diagnosed with increasing frequency, according to Theodore Winship and William W. Chase<sup>5</sup> (Washington, D C ), who studied 285 cases collected from the literature or found by a survey conducted in the United States, Canada and western Europe, 64.8% of the children were girls. The age at which histologic diagnosis was made ranged from 4 weeks to 14½ years, the average being 9.8 years. The average patient had a nodule in the neck at the age 7. If growth rate is uniform, it is apparent that thyroid carcinoma may begin at an early age, five children had a thyroid tumor at birth. Of 145 nodular goiters, 29% were carcinomatous. Cervical lymph node metastases were present in 64% of the patients when first treated, and in 18% of these the metastases were bilateral. Pulmonary metastases were seen in 15% when first examined and eight patients had osseous metastases. Only two patients had symptoms of hyperthyroidism.

Of 116 patients, 16 had had x-ray treatment for enlarged thymus gland. This is a considerably higher prevalence rate of thyroid carcinoma than would be expected in a group of nonirradiated children. In a group of 1,400 patients treated by radiation during infancy for enlarged thymus, Simpson and associates found 17 in whom malignant disease subsequently developed, 6 of them had thyroid carcinoma.

The prognosis for children with thyroid carcinoma is poor. In the authors' series, 48 (16.7%) died of the disease, 9 shortly after operation and the others after variable periods, up to 23 years. That tumors containing papillary elements caused 65% of the deaths, follicular carcinoma 22% and undifferentiated carcinoma 13% suggests the need of prompt and adequate therapy for children with thyroid carcinoma, regardless of the cell type.

Recurrences after long quiescence suggest that follow-up study of under 20 years in patients with thyroid carcinoma is of relatively little value. Results of the study corroborate



the work of others in disproving the impression that carcinoma grows faster in children than in adults

**Papillary Thyroid Carcinoma: Pathologic Findings in Cases with and without Clinical Evidence of Cervical Node Involvement.** Edgar L. Frazell and Frank W. Foote, Jr.<sup>6</sup> (Memorial Center for Cancer, New York) examined 182 specimens from radical neck dissections for papillary thyroid carcinoma. In 104, the neck nodes were clinically diagnosed as containing cancer and in 11 others diagnosis was doubtful. Of these specimens, 113 had histologic proof of metastases in one or more nodes. In an additional 67 specimens with no clinical evidence of cervical node metastases, 41 contained metastases when examined histologically.

Patients with no clinical evidence of cervical node metastasis were four times more likely to have metastases limited to a single area than those with clinical signs of local metastases. Radical neck dissection removes the lymph nodes in the region of the submaxillary triangle, the upper, middle and lower portions of the deep internal jugular chain and the spinal accessory chain. The nodes that lie in close relation to the thyroid capsule and below the thyroid gland, extending to the mediastinum, should be studied more completely.

Papillary carcinoma is the most common form of thyroid cancer. Microscopically, there are follicular as well as papillary qualities. The tumors occur in all age groups and are notorious for slow rate of clinical growth, regardless of treatment. The proper therapeutic approach is difficult to determine. It is important to realize that these papillary carcinomas, although slow growing, do kill.

Even when the neck was clinically negative for metastases, node metastases were found histologically in 61%. This does not settle the issue of whether radical neck dissection is indicated in thyroid carcinoma. However, if the surgeon favors a radical surgical approach he must include in consideration for the operation patients who have no clinical evidence of cervical node metastases. If he does not include these patients, he knowingly leaves behind removable local lymph node metastases in some 60% of his patients. Whether this logic will be practical remains for the future to prove. Extremely long term follow up studies will be required.

**Pathologic Physiology of Carcinoma of Thyroid** Robert C. Horn, Jr.<sup>7</sup> (Univ. of Pennsylvania) states that thyroid carcinoma is quite a variable disease. Its incidence is about 0.5% of all carcinomas. About 89% of all nodular lesions of the thyroid are carcinoma. Unsuspected cancer is found in 53% of surgically treated nodular goiters. There is much confusion regarding the nature of the relationship of nodular goiter to cancer. The figures do not imply that carcinoma arises in a nodular goiter. The evidence for believing that many thyroid carcinomas arise in adenomas is far from conclusive. The common slow evolution of many thyroid cancers indicates that many thyroid nodules may exist as malignant tumors over long periods of time and need not be interpreted as malignant change supervening in a pre-existing benign lesion. Toxic goiter is infrequently associated with cancer.

The peak incidence of thyroid cancer is in the fifth decade, and two thirds of the patients are aged 41-70. Thyroid carcinoma may be of long duration before diagnosis, and many patients diagnosed in the second or third decade of life actually had thyroid cancer when they were in their first or second decade. The incidence of thyroid cancer in thyroid nodules is very high in young patients. Thyroid cancers have a low grade of malignancy in younger patients and a high grade of malignancy in older patients. The relative predominance of thyroid cancer in the female is between two and four to one.

The classification of 189 cases of thyroid cancer was low degree of malignancy in 72% (including malignant adenoma, 13%, follicular, 19%, papillary 33% and mixed papillary and follicular, 7%), intermediate degree of malignancy (adenocarcinoma) in 19%, high degree of malignancy (undifferentiated) in 8% and miscellaneous malignant tumors such as epidermoid carcinoma and sarcoma.

Malignant adenoma differs from the more common benign adenomas in certain histologic features, often of minor degree. They tend to be more solidly cellular, there may not be good follicle formation and little colloid is present. The tumors tend to invade blood vessels, and bone and lung metastases are common. The tumor grows slowly and a long term follow up is necessary. Follicular carcinoma par-

(7) S. Clin. North America 35:1669-1681, December 1955.

allels papillary carcinoma in its clinical evolution and frequently occurs in mixtures with it. Papillary carcinoma is the most common of the thyroid carcinomas. Papillary and follicular tumors usually spread via the lymphatic channels and the most frequent site of metastasis is the cervical lymph nodes. The tumors tend to be multicentric. Papillary and follicular thyroid cancers tend to have a prolonged clinical course. Lateral aberrant thyroid carcinoma usually if not always, represents cervical lymph node metastasis from an occult primary carcinoma in the thyroid proper. These tumors are usually papillary or follicular, or a mixture of both. The nonencapsulated sclerosing tumor should be classified with papillary or papillary and follicular tumors.

Adenocarcinomas, tumors of an intermediate degree of malignancy, resemble follicular carcinomas but are less well differentiated in varying degree. The best known and most striking of the undifferentiated thyroid carcinomas is the giant cell or spindle cell carcinoma. Survival of patients with this tumor is rare.

The functioning of thyroid carcinoma—its ability to collect radioactive iodine—parallels the differentiation of the tumor, particularly with respect to the amount of colloid present.

The 5 and 12 year survivals of patients with thyroid cancers were respectively, malignant adenoma, 56% and 25%; papillary follicular or mixed 74% and 38%; adenocarcinoma 54% and 33%; and undifferentiated, 19% and 12.5%. The results indicate the variability of the course of the types of disease and the necessity of following patients for a long time. Patients who survive for five years may later die from the disease.

**Postoperative Hypoparathyroidism.** On the basis of a study of 50 patients (mean age, 39, 43 females), Joseph A. Buckwalter, Robert T. Soper, Jack Davies and Edward E. Mason<sup>8</sup> (State Univ. of Iowa) cite the need for re-examination of current clinical concepts that parathyroid deficiency is usually transient and presents no particular therapeutic problem. Permanent parathyroid deficiency following thyroid surgery is not infrequent; management is often difficult and incapacitating complications are not uncommon even in patients under medical surveillance. Progression to late irre-

versible sequelae, which include cataract, convulsive disorders and mental deterioration, can occur in a patient who has continuing uncontrolled hypoparathyroidism although displaying none of the common stigmas of the disorder.

Because parathyroid glands are usually imbedded in adipose tissue and their anatomic relation to other cervical structures is inconstant, identification at operation is difficult. This explains unexpected development of tetany following subtotal thyroidectomy. Interference with blood supply, derived chiefly from inferior thyroid arteries, is probably the cause of transient hypoparathyroidism. Bilateral extracapsular ligation of inferior thyroid arteries was done in 19 of 37 patients operated on at University Hospitals. Total parathyroidectomy is exceptional with total thyroidectomy, as done for cancer, probably because one or more parathyroid glands may be located deep in the tracheal esophageal groove.

In a patient with recent thyroid surgery, tingling, paresthesias and numbness, and tonic spasms of fingers and toes, along with increased neuromuscular irritability, are pathognomonic of parathyroid insufficiency. Tightness and stiffness of other muscle groups, feeling of restricted breathing, hyperventilation and laryngospasm are less frequent and usually appear later. Laboratory tests show depression of calcium and elevation of phosphorus in serum and decreased or absent calcium in urine. Diagnosis is confirmed by prompt disappearance of symptoms when calcium is given intravenously.

Vitamin D<sub>2</sub> (50,000-200,000 units daily) and calcium lactate powder orally (5-15 Gm daily) should be started immediately, with a low phosphorus diet. For the exceptional resistant case, dihydrotachysterol (A. T. 10) may be used. Periodic discontinuance of treatment is necessary to determine whether the disorder persists. No patients in whom it persisted a year or more reverted to normal. Of 33 patients, 25 had permanent and 8 transient hypoparathyroidism.

Late in the course, absence of symptoms and signs when treatment is discontinued does not necessarily mean normal parathyroid function. The only indication of persisting deficiency may be marked depression of serum calcium and increased serum phosphorus. Final tragic confirmation "

too often provided by serious late complications. Cataracts, which occurred in 10 patients, were noted one year after operation in a patient with uncontrolled hypoparathyroidism. Several of seven patients with cataract operated on elsewhere were referred for treatment without recognition of the hypoparathyroid state. Hypoparathyroidism was not recognized in another patient (who died at age 38 with myocardial fibrosis) as the probable cause of a convulsive disorder and mental deterioration.

Time and character of onset, early clinical pattern and response to treatment could not be related to these late sequelae nor to transient or permanent nature of the disorder. To avoid such late complications, treatment must be continued until serum calcium and phosphorus levels remain normal and clinical remission persists during a prolonged trial without therapy.

Occurrence of Thyroid Cancer in San Francisco, 1950-53, was analyzed by Merrill J. Alexander<sup>9</sup> (V.A. Hosp., San Francisco). A previous statistical hypothesis would allow 20 cases in a community of 800,000, with 10 new cases diagnosed each year and 5 deaths each year. Actual incidence was 26 per year, and prevalence rate was far in excess (at least 400%) of the hypothetical value of 20. Deaths per year exceeded the hypothetical value by at least 40%.

During each of the four years studied, occurrence of cancer of the thyroid increased steadily, possibly indicating increasing awareness and greater dispatch in surgical management of nodular goiter. Removal of a thyroid nodule found on routine physical examination often demonstrated carcinoma. Cases with metastases also increased proportionately, indicating that diagnosis is not being made earlier, although more cases are being discovered.

This type of cancer is especially one of youth to middle age. Tendency to metastasize, though especially marked in the teens, otherwise roughly parallels occurrence. Papillary carcinoma proved to be appreciably more common than adenocarcinoma only in the third decade. Before age 30, both types proved much more malignant than either lesion in middle life. Metastases were present in all patients in the second decade. Metastases occurred most often to regional lymph nodes and were equally invasive into surrounding

muscles and trachea. For papillary adenocarcinoma, muscles were involved in 4, trachea in 2 and lymph nodes in 13. For adenocarcinoma, corresponding numbers of cases were 4, 4 and 12, respectively.

Treatment of cancers in most cases was curative in intent. Extent of surgery paralleled extent of the lesion and its metastases in most cases. Bilateral radical neck dissection in addition to total thyroidectomy was performed in four patients. One was given I<sup>131</sup> therapeutically.

Prognosis depends on type of carcinoma, age of patient, extent of disease at initial treatment, extent of surgery and radiosensitivity. Although Crile considers carcinoma to be of low malignancy in patients under 40, in this study it appears that lesions are as malignant in young patients.

**Parathyroid Crisis.** Treatment of Emergency Parathyroidectomy. Philip R. James and Paul G. Richards<sup>1</sup> (U. S. Naval Hosp., Corpus Christi, Tex.) review 14 cases of parathyroid crisis from the literature and add a case of their own. Chronic hyperparathyroidism may undergo an acute exacerbation, with a high mortality. Onset of parathyroid crisis may be heralded clinically by epigastric pain, vomiting, lethargy progressing to coma, oliguria, hyperpyrexia and vascular collapse. Rising serum phosphorus and non-protein nitrogen levels may indicate impending parathyroid intoxication.

The pathophysiologic mechanism producing the acute crisis is poorly understood. In several reported cases use of a high calcium absorbable alkali regimen had an adverse effect on the course of the disease. In addition, prolonged immobilization with skeletal demineralization may precipitate an acute crisis in chronic hyperparathyroidism by aggravating a pre-existent metabolic dysfunction. The possibility of adrenal cortical exhaustion from stress associated with chronic hyperparathyroidism is considered a possible mechanism in the acute crisis.

Acute primary hyperparathyroidism, or, more properly, an acute exacerbation or crisis in chronic primary hyperparathyroidism is a surgical emergency necessitating parathyroidectomy. When hyperparathyroidism is suspected, a low calcium intake should be maintained, undue immobilization avoided and serum electrolyte abnormalities cor-

(1) A.M.A. Arch. Surg. 70:553-566, 1956.

rected to prevent dehydration and alkalosis. These factors enhance calcium precipitation in the renal tubules and may lead to acute renal insufficiency.

In 80-85% of cases, hyperparathyroidism is due to a solitary adenoma. In 5-10% there is more than one adenoma and in 10% there is diffuse hyperplasia of all four parathyroid glands. Most parathyroid adenomas will be yellowish brown or reddish brown and will have a definite capsule, with a more or less well defined hilus through which delicate blood vessels enter. The adenoma will be oval or globular, and it may appear flattened if compressed by neighboring structures.

If a mass is present near the thyroid gland, surgical exploration should begin there. If there is no mass, it makes no difference which lobe of the thyroid is mobilized first. The important features of dissection are good exposure of the thyroid, extensive mobilization of the lobes and careful attention to hemostasis. The most constant place to find the superior or true parathyroid is where the recurrent laryngeal nerve passes under the lowermost fibers of the inferior constrictor muscle as they attach to the horn of the thyroid cartilage. The inferior parathyroid is most constantly found at the point where the inferior thyroid artery enters the posterolateral aspect of the body of the thyroid gland. Either of the parathyroids may become displaced into the mediastinum. If a diffusely hypertrophied parathyroid is found, subtotal resection of the glands should be done.

Postoperatively, a transient tetany may almost always be expected and is combated by calcium gluconate intravenously. Postoperative oliguria indicates that all the hyperfunctioning parathyroid tissue was removed.

Failure to recognize the disease and failure to deal with it promptly when it is first recognized will lead to a high mortality.

**Thyroid Activity during Operation** was studied by Ira S. Goldenberg, Leo Lutwak, Paul J. Rosenbaum and Mark A. Hayes<sup>2</sup> (Yale Univ.) in 17 operations among 16 patients aged 35-78. Each patient received a tracer amount of  $I^{131}$  48-72 hours before operation, permitting equilibration and maximal protein binding. 24-hour uptake of  $I^{131}$  was used as evaluation of preoperative level of thyroid activity. On

the day of operation, blood samples for protein-bound radioiodine (PBI<sup>131</sup>) determinations were drawn before and after preanesthetic medication, during induction of anesthesia, during operation at intervals of 20-45 minutes, at tracheal extubation and when the patient was fully awake, usually 1-2 hours postoperatively. Several patients also had serial postoperative PBI<sup>131</sup> determinations.

Increase in conversion ratios after onset of surgical trauma corroborates previous observations suggesting increased thyroid activity, apparently a normal response. When chronic hemorrhage, debilitating illness, poor nutrition and weight loss are present, thyroid response is decreased or absent. Effects of acute stress in altering metabolic-endocrine responses to subsequent episodes of trauma are also important. Patients who had surgical procedures shortly before a second operation (studied with PBI<sup>131</sup> levels) did not show thyroid activation after the second operation. One patient studied during two operations responded with thyroid activation after the first but showed no response after the second.

Preoperative level of thyroid activity appeared to influence stress response. Patients with glandular uptake of radioiodine of 40% or more after 24 hours (high euthyroid) had much greater thyroid activation in general than those with uptake under 40%. Age and degree of trauma apparently had little effect.

After an increase in conversion ratio early in the operation, a fall to preoperative or lower than preoperative levels followed in most patients, suggesting decrease in production of thyroid hormone or increased utilization at the cellular level and perhaps also pronounced adrenocortical responses. In four patients in whom conversion ratios never returned to preoperative levels adrenocortical response may have been lacking. Stability of hematocrit and total protein determinations suggest that neither blood dilution nor alterations in protein composition present for iodine binding altered the results.

**Treatment of Thyrotoxicosis with Thiouracil Compounds**  
A Jervell, G Qvigstad, and O Ytrehus<sup>3</sup> (Tonsberg Norway) state that of 232 patients with thyrotoxicosis 41 had primary surgery, 21 had secondary surgery and 153 were

(3) Acta chir scandinav 110 93 106 1955



successfully treated with thiouracil compounds. Lugol's solution was given to 17 patients. The first drug given was methylthiouracil in an initial dose of 0.2 Gm. three times daily with subsequent reduction according to degree of clinical improvement. If the drug caused reactions, it was replaced with propylthiouracil in doses of 0.1 Gm. three times daily. The maintenance dose of methylthiouracil after six months was usually 0.1 Gm. one to seven times a week and that of propylthiouracil was correspondingly lower.

Of 174 patients treated with thiouracil compounds, 21 abandoned the drug for surgical treatment. Thiouracil compounds were given to 78 patients for one to three years then discontinued, and the patients were followed up to two years without recurrence, 75 continued treatment.

Indications for surgery were marked thyroid enlargement in 33, suspected cancer (not found) in 2, thyrotoxic adenoma in 3, toxicity from thiouracil in 7, difficulty of medical supervision in 12 and recurrence after medical treatment in 5. Absolute indications for medical treatment can scarcely be said to exist. There were 53 patients especially suited for medical treatment, including 6 over age 75, 15 with recurrence after surgery and 32 with only slight thyrotoxicosis. In 138 cases there were no definite indications with regard to choice of treatment.

Surgery was used in 171 patients without death. Operative complications included tetany in 2.3%, recurrent nerve paralysis in 7.1%, hypothyroidism in 5.3% and persistent thyrotoxicosis or recurrence in 4.7%. The results of surgery were quite satisfactory in 92.4%. The operative treatment of thyrotoxicosis is an extremely effective method involving negligible mortality risk but it does involve the risk of complications most of them innocent but some serious. When successful, the method offers the prospect of immediate cure and much will have to be obtained from medical treatment before it becomes a competitive method.

Deaths ascribable to antithyroid therapy did not occur, although four patients died while under observation. Toxic reactions occurred in 24% of patients receiving methylthiouracil and in 2% of patients receiving propylthiouracil. Serious reactions occurred in only one patient. Side effects included fever in 32, malaise, headache and vomiting in 19, leukopenia in 12, joint pain and agranulocytosis in 4 each,

exanthema in 5, and tonsillitis and thrombocytopenia in 1 each. Most of the toxic reactions occurred during the first two weeks of therapy.

The risks involved in antithyroid therapy with thiouracil and iodine compounds are minimal and undoubtedly smaller than those involved in surgical treatment. The incidence of recurrence with medical therapy was more than twice as great as that following surgery. The greatest disadvantage of medical therapy is that it must be continued over long periods.

**Carcinoma of Thyroid Gland in Children.** Alvin B. Hayles, Roger L. J. Kennedy, Oliver H. Beahrs and Lewis B. Woolner<sup>4</sup> (Mayo Clinic and Found.) report on 10 boys and 31 girls under age 15 with carcinoma of the thyroid between 1909 and 1954. Peak age at diagnosis was 13, and average duration of symptoms before diagnosis was  $2\frac{1}{2}$  years. All patients had a palpable mass in the neck not associated with preceding infection or systemic reaction. Two had respiratory obstruction, 1 had hoarseness and 33 had palpable cervical lymph nodes. Metastatic involvement of both sides of the neck was found in nine during the course of the disease. Lymph nodes involved with thyroid carcinoma are firm, usually movable, nontender and discrete and in most cases are members of the tracheoesophageal or jugular chain. Most nodes were between 1 and 2 cm. in diameter, and fixation or matting was seen only late in the disease.

Abnormalities of the thyroid gland on palpation were found in 38 patients. In some cases the gland was diffusely or slightly enlarged or firmer than normal, but in most a firm, nontender nodule was palpated. Both lobes were involved in nine patients.

All the carcinomas were of the slowly growing type, with a low grade of histologic malignancy. Papillary and follicular carcinoma was found in 36, and regional lymph nodes were involved in 32 of these. Pulmonary metastases occurred in eight and bone metastasis was suspected in one. Five patients had an encapsulated tumor called "malignant adenoma."

All lesions should be explored and at least biopsied. The lateral cervical region should be examined carefully for evidence of metastases. If there is a carcinoma, total lobec-

(4) A M A J Dis Child. 90:705-715. December 1955.

tomy on the side of the lesion should be performed and involved lymph nodes removed. Radical dissection of the neck is not necessary, but a modified cervical dissection with excision of the involved nodes should be done. Metastatic papillary carcinoma from the thyroid tends to remain encapsulated for a long time. Later removal of involved nodes may be necessary. If the carcinoma is well localized, only partial lobectomy is performed on the contralateral side in addition to lobectomy on the affected side. The partial lobectomy preserves thyroid tissue for normal function and protects corresponding parathyroid glands. If the carcinoma is located in the isthmus of the thyroid gland, subtotal thyroidectomy should be done, leaving a remnant on either side equal to less than one fourth of a normal lobe.

If distant metastases are present or the primary lesion is very extensive, total thyroidectomy should be done to facilitate the use of radioactive iodine, though it carries the danger of parathyroid insufficiency. Radioactive iodine is useful for inoperable or metastatic thyroid carcinoma, with the normal thyroid tissue removed so that it will not compete with the carcinoma tissue for radioactive iodine. Roentgen ray and radium therapy are reserved for inoperable lesions that do not respond to radioactive iodine.

Surgical excision of the thyroid nodule followed by external irradiation was done in seven patients without metastases. Subtotal thyroidectomy with excision of cervical lymph nodes was performed in 21 and total thyroidectomy in 4. Three were treated with x-rays or radium alone. Six cases were considered inoperable.

There were no operative deaths. Six patients had died 21, 20, 18, 11, 7 and 1 year, respectively, after the diagnosis was made. Five of the six had widespread pulmonary metastases. Hypothyroidism occurred in 13 patients, in 6 as part of the treatment plan. Hypoparathyroidism occurred in all four patients subjected to total surgical thyroidectomy.

**Results of Conservative Operations for Malignant Tumors of Thyroid.** George Crile, Jr., Julian G. Suhrer, Jr. and John B. Hazard<sup>5</sup> (Cleveland Clinic) state that excellent results may be obtained by conservative operations on most papillary carcinomas of the thyroid and their follicular variants provided the primary tumor is completely excised.

and grossly involved groups of lymph nodes are removed

Of 107 patients with papillary carcinoma of the thyroid, 33 had had a previous operation on the thyroid (secondary group) and 74 had not (primary group). Carcinoma in the thyroid and cervical lymph node metastases were found in 63.5% of the primary group and in 66.6% of the secondary group, figures for carcinoma in the thyroid without cervical lymph node metastases were 36.5% and 0%, for lymph node metastases without carcinoma in thyroid 0% and 33.3%, and for distant metastases, 5.4% and 9.1%.

The extent of surgery in the primary group was removal of primary tumor and lymph nodes in 62.2%, removal of primary tumor only in 36.5% and biopsy of cervical node only in 1.3%. Types of operations in the primary group were total thyroidectomy in 16.2%, total lobectomy in 56.8%, partial lobectomy in 21.7%, bilateral subtotal thyroidectomy in 4% and biopsy of cervical node only in 1.3%. The extent of surgery in the secondary group was removal of primary tumor and lymph nodes in 57.6%, removal of lymph nodes only in 33.3%, biopsy only in 6.1% and palliative resection of the thyroid in 3%. The types of operations in this group were total thyroidectomy in 15.1%, total lobectomy in 36.4%, partial lobectomy in 6.1%, unilateral removal of lymph nodes only in 18.2%, bilateral removal of lymph nodes only in 3%, palliative excision of part of thyroid tumor in 3%, excision of solitary cervical node or mass in 12.1% and biopsy only in 6.1%.

Average follow-up period in the primary group was 4½ years. Of these, 82.4% were living without evidence of carcinoma, 6.8% died without evidence of recurrence, 4.1% were lost to follow up but had no evidence of recurrence when last observed, 4.1% were living with distant metastases present preoperatively, 1.3% died of their carcinoma and 1.3% died of other causes but with distant metastases. The average follow-up period in the secondary group was three years. Of these, 69.8% were living without evidence of carcinoma and 3% died of other causes without evidence of carcinoma, 3% were living with local recurrence, 3% with local recurrence and distant metastases, 3% with distant metastases present preoperatively, 3% with distant metastases that developed after surgery, 12.2% died of the disease and 3% died of unknown causes. Among 81 patients

cases Enlargement of the thyroid gland could be detected by palpation in five patients, and three others had had previous thyroid surgery A positive diagnosis can be made preoperatively only by the use of radioactive iodine

Surgical removal of a posterior mediastinal goiter is simple if it is small The cervical portion of the thyroid gland is removed in the standard manner through a collar incision and traction on the intrathoracic extension results in its delivery into the neck

The anatomic relationships of a large goiter are important in its safe removal Simple traction cannot be used for large tumors because of the danger of tearing the large vessels that lie anteriorly The anterior aspect of the goiter is the only one accessible to the surgeon If a finger or instrument is thrust through the thoracic inlet along the front of the tumor in an attempt to lift it into the neck there is danger of massive hemorrhage from the innominate veins or vena cava Attempts to extract large thyroid masses from the thorax after their bulk has been reduced by piecemeal removal of the contents is successful when the mass is cystic but there is always danger of bleeding from inferior thyroid veins that cannot be secured before the tumor is delivered Severe bleeding from the superior and inferior thyroid arteries may result when fleshy pieces of thyroid tissue are removed from the thoracic portion of the gland even if vessels are ligated Thoracotomy alone is not successful because the cervical part of the gland is not touched, and the difficulties associated with removal of the goiter involve the thoracic inlet, where the pedicle to the tumor is hidden

A good surgical approach is combined thoracotomy and cervical operation A better approach is the addition of a sternum-splitting incision to the standard cervical operation Splitting the sternum and retracting widely brings the whole operative field into view The cervical stage of the operation results in mobilization of the thyroid lobe from which the mass has arisen The pedicle connecting the cervical and thoracic portions of the thyroid can be traced down to the apex of the goiter, protruding above the innominate vein tightly stretched across its anterior surface The great vessels are displaced easily and carefully and the goiter delivered onto the surface Should a mishap occur, the whole field is under direct control

► [From personal experience the editor also can recommend a sternum splitting incision for these cases—Ed]

**Radioactive Iodine or Surgery in Treatment of Hyperthyroidism** Dwight E. Clark and James H. Rule<sup>8</sup> (Univ of Chicago) have treated 700 patients during the past eight years. Criteria for  $I^{131}$  treatment were uncomplicated hyperthyroidism in patients over age 40, recurrent or persistent hyperthyroidism after thyroidectomy, hyperthyroidism with severe cardiovascular disease or other concurrent disease, failure to respond properly to antithyroid drugs, refusal to accept surgery or other therapy or severe exophthalmos. Contraindications include pregnancy and lactation, clinical solitary nodule with hyperthyroidism, nontoxic nodular goiter and nontoxic diffuse or simple goiter. Because of the strong possibility of an existing carcinoma, patients with hyperthyroidism and a clinically solitary nodule should have surgery with or without  $I^{131}$  unless the nodule can be proved to be a hyperfunctioning adenoma. Several patients had solitary nodules, in a few of whom they disappeared as hyperthyroidism was controlled. If the solitary nodule persisted after euthyroidism was established, surgery was strongly recommended.  $I^{131}$  will not appreciably alter the size of a nontoxic nodular goiter, and such conditions should be treated surgically if therapy is indicated.

Of 628 patients with hyperthyroidism treated with  $I^{131}$ , 520 became euthyroid and 108 hypothyroid. Complete remissions were obtained in 81.6% after one or two therapeutic doses. Only one dose was required in 56.1% for a remission, two doses in 25.5% and three or more in 18.4%. No patients had radiation sickness and there was no evidence of bone marrow depression or injury to parathyroids, kidneys or bladder. Menstrual abnormalities did not occur, and several women subsequently delivered healthy children.

Untoward effects are minimal. A moderate number of patients have noted tenderness in the region of the thyroid gland for several days to a week and some noted a sensation of constriction in the neck five to six weeks after therapy and continuing for a considerable period. The actual incidence of significant hypometabolism (11%) was comparable to that after surgery.

In selected cases of thyrotoxicosis,  $I^{131}$  therapy has many

advantages over surgery. There is no mortality, no parathyroid destruction and no recurrent nerve damage. Compared with surgery, the cost is relatively inexpensive. No hospitalization is required, virtually no time is lost from work, administration is painless and the cosmetic result is excellent. Recurrence rate is negligible, and the isotope should be effective in all cases of true hyperthyroidism if given in adequate amounts.

**Chronic Thyroiditis and Riedel's Struma—Etiology and Pathogenesis: Role of Hyperfunctioning Parenchyma of Primary Hyperplastic Goiter.** According to Emil Goetsch and Mildred Kamner<sup>9</sup> (New York), chronic nonspecific thyroiditis is an inflammatory response to etiologic irritative factors residing in the hyperfunctioning epithelium of primary hyperplastic (toxic diffuse) goiter. Actual etiology is still unknown. From incipency to terminal stage of generalized fibrosis, it runs a protracted course and is characterized by great variability in histologic features. The course is divided into incipient, early, intermediate and terminal phases.

Onset of chronic nonspecific thyroiditis is characterized by circumscription, isolation and progressive destruction of numerous irritative foci of hyperfunctioning parenchyma by lymphoid and plasma cells. The incipient qualitative pattern continues through several successive stages and develops into a massive quantitative one. By gradual transition over protracted periods the inflammation advances to a terminal stage in which there is virtually complete destruction of the thyroid parenchyma and replacement by fibrous tissue. The lesion need not always advance to the terminal stage, and the pathologic process may be halted at any time during its course. Otherwise the terminal stage would occur oftener.

The authors agree with Levitt, who described six phases, from epithelial hyperplasia to the terminal stage of fibrosis typical of Riedel's struma. The phases were naturally not sharply delineated but progressed gradually from one to the next. The limited areas of fibrosis in one phase became the predominant feature of the next, e.g. the restricted areas of advanced inflammation of the intermediate phase to a considerable extent, assumed the histologic appearance of Riedel's struma.

(9) J. Clin. Endocrinol. 15 1010 1034. August, 1955

The time required for development of Riedel's struma from early thyroiditis is necessarily protracted and variable, embracing (1) initial period of hyperthyroidism followed by (2) amelioration of symptomatology and (3) gradual transition toward state of hypothyroidism.

## THE BREAST

**Mammary Cancer—The Other Breast.** According to Ray Lawson<sup>2</sup> (Royal Victoria Hosp., Montreal), some surgeons

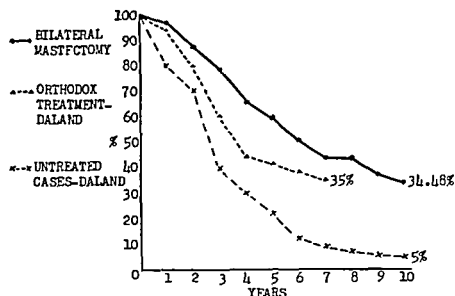


Fig 18—Survival curve of 32 patients with bilateral mastectomy 16 living, 16 dead (Courtesy of Lawson, R Canad M A J. 73 676 677, Oct 15, 1955)

advocate the prophylactic removal of the other breast because (1) 7.5% of the patients subsequently develop contralateral cancer, (2) the same etiologic factors influential in the development of cancer in one breast are probably active in the opposite breast and (3) the same genetic and hormonal factors exist. Whether the cancer that develops in the second breast is primary or metastatic cannot be answered.

In 100 consecutive autopsies of women who had had breast cancer, gross cancer was found in the opposite breast in 13, and 8 had had mastectomy because of cancer in the

(2) Canad M A J 73 676 677, Oct 15, 1955



second breast. The other breast had not been examined in 22 patients, and so the incidence of contralateral breast cancer was probably higher than 21%.

Of 547 patients who had surgery for breast cancer, 32 had both breasts removed, 16 of the 32 were alive at the end of 10 years (Fig 18). After the first operation, the average survival time of the living patients was 9 years 7½ months, of those who died, 7 years 1 month. Of the 32, 19 had gross axillary metastases at the time of operation, and of these, 9 were alive at follow-up, with an average survival of 9 years 4 months. The 10 who died survived an average of 7 years 2½ months. The average survival time in 19 cases of proved bilateral breast cancer was 7 years 7 months.

Removal of the opposite breast improves survival time.

**Preoperative Roentgen Therapy with High Doses Followed by Radical Surgery for Cancer of Breast: Ten Year Follow-up.** F. Baclesse<sup>3</sup> (Paris) reports results in 77 patients treated during 1935-46. 3 had local recurrence after conservative mastectomy elsewhere and 74 had received no previous treatment. After 5 years, 34 (44%) were apparently cured, and after 10 years, 27 (35.5%), i.e., the tumor and axillary and subclavicular lymph node involvement had disappeared and there were no clinical or radiologic signs of metastases. Two patients lost to follow-up were counted as dying of cancer.

Histologic examination of operative specimens after irradiation showed 9 completely "sterilized," 9 with doubtful "sterilization," 23 modified and 36 with little change in cancer cells. Postoperative histologic findings are important in prognosis. In the more advanced cases, notably stage III and advanced stage III, radical operation becomes mostly useless, since distant metastases are fatal and only a small number of patients benefit (those with histologically "sterilized" or "doubtful" specimens).

Almost all patients were treated with 180 kv, 1 mm Cu, 50-60 cm skin distance, 15-20 r/minute, some had 250 kv, 1 mm Cu filtration. Only with skin doses beyond 4,000 r through two opposing fields are chances of "sterilization" good. These doses, the limit of tissue tolerance, must not be exceeded in breast and axillary regions if postoperative complications are to be avoided. For the "radiotherapy seg

ment" (internal mammary chain and supraclavicular region), doses should be higher

With the use of sound radiotherapeutic principles (well defined fields, alternation of fields and adequate daily doses within tissue tolerance), operation can be performed under satisfactory conditions, with added safety furnished by antibiotics. The time interval between the end of roentgen therapy and operation depends, among other factors, on the dose administered, the smaller the dose, the shorter must be the interval. On the average, and for doses advocated, it may be set at two or three months. This delay will permit slowly acting cancerocidal effects of radiation to exert maximal influence. Mammography is considered important for estimation of the extent of necessary surgical and radiotherapeutic procedures and for prognosis.

**Cancer of Male Breast.** Report of 146 Cases. Norman Treves and Arthur I. Holleb<sup>4</sup> (Memorial Center for Cancer, New York) present 146 histologically confirmed cases of breast cancer in men, aged 24-85 (average, 52.1). The patients were 96% white, and European-born Jews comprised 37%. The left breast was involved more frequently than the right. Bilateral cancer was found in 27% and associated significant primary cancer of another anatomic site in 54%. No relationship could be established between breast cancer and trauma or pre-existing benign breast disease.

In more than two thirds the first symptom was a breast mass. True nipple discharge was common. Median duration of symptoms before medical care was sought was nine months. About two thirds of the patients were classified as operable. The finding of a mass in the adult male breast warrants suspicion of a malignant tumor, when the mass is associated with nipple discharge, the diagnosis is almost assured. Biopsy is indicated.

Most of the tumors were infiltrating duct carcinomas. Except for lobular carcinoma and cystosarcoma phyllodes, all pathologic types found in the female breast were encountered. Nipple discharge was more often associated with an infiltrating duct carcinoma than with a papillary carcinoma.

Radical mastectomy was performed in all who could stand major surgery. There was one postoperative death. Castra-

(4) Cancer 8:1239-1250, Nov-Dec, 1955

tion was performed for palliation in more than 30 patients. Its results will be reported later. If only patients who were known to be clinically free from disease five years after treatment are considered as having successful results, the survival rate is 29.1%. If only operable cases are considered, the five year survival rate is 41.9%. If the determinate cases within the primary operable group are evaluated, the rate is 55.7%. Almost all patients in the inoperable category died within two years of hospitalization.

Papillary breast cancer in the male seems to offer an excellent prognosis. The six determinate patients with this type survived five years without recurrence and none had proved axillary metastases. The five year survival pattern of the commoner infiltrating duct carcinoma paralleled that of breast cancer in the female. When the homolateral axillary lymph nodes were invaded, the survival rate dropped to 30%, as opposed to a rate of 75% when the tumor was confined to the breast. The age of the patient did not seem to influence the end results, prognosis being more dependent on type of cancer and presence or absence of metastases in axillary lymph nodes.

**Postmastectomy Lymphedema** Ian Macdonald and Kent Osman<sup>5</sup> (Univ. of Southern California) determined the disparity of arm measurements 10 cm below the acromion process in a control population of 100 normal women, to provide a standard of reference for estimating postmastectomy edema. The mean circumference of the right arm was 27.541 cm and of the left arm, 27.182 cm, indicating that both arms are practically the same. The degree of edema was measured in the same manner in 143 postmastectomy patients. 53 had had resection of the axillary vein and 82 received postoperative irradiation. All patients with axillary node involvement were treated by irradiation in a tumor dose of 3,000-3,500 r, half-value layer 1.0 mm Cu, to axillary and supraclavicular areas.

Conventional radical mastectomy alone caused some swelling of the arm in 40-60% of the patients. Axillary vein resection did not increase the postmastectomy swelling of the arm over conventional radical mastectomy. Irradiation, however, did increase the postmastectomy swelling. Irradi-

(5) Am J Surg 90:281-286 August 1955

ation causes swelling by lymphatic blockage; therefore, postmastectomy swelling is true lymphedema.

Serial venograms in 10 postmastectomy patients with and without edema failed to demonstrate significant abnormalities in the axillary vein or its tributaries.

Occlusive pressure dressings have been abandoned by the authors in postoperative care of mastectomy patients because they provide an ideal bacterial medium and keep the skin flaps artificially moist and unhealthy. Preliminary results in the immediate postoperative management of 14 patients by omission of all dressing and constant suction drainage with a Foley catheter in the lower axillary area have been excellent. The patients were followed for three months; 10 had primary healing and 4 had healing delayed by minor areas of wound separation. None had major necrosis and prolonged healing. Nine had edema of the arm of 0.75 cm. or less and only two had swelling of 2 cm. or more.

**Fixation of Skin Flaps by Subcutaneous Sutures in Radical Mastectomy** significantly decreases surgical morbidity, according to Bernard B. Larsen<sup>6</sup> (Western Reserve Univ.), who describes a technic he has used satisfactorily in 25 consecutive cases.

**METHOD**—An elliptical incision is usually preferred, with the upper limit going obliquely across the axilla toward the posterior axillary fold, because this affords a large upper skin flap to close over the axillary region. After radical amputation is accomplished, the arm is placed in abduction and skin flaps are then simply fixed to chest wall and axilla by 35-50 subcutaneous fine cotton sutures to deep muscles and fascia (Fig. 19). In covering axillary vessels, the upper flap is sutured first to the remaining clavicular portion of the pectoralis major muscle, then to chest wall in the region of 1st and 2d ribs and then to adjacent deep muscles. The flap is thus pulled high into axillary fossa, obliterating all major potential dead space. The arm held in marked abduction facilitates this part of the closure. Remaining flap areas are fixed to chest wall by subcutaneous sutures about 5 cm. apart. Skin edges are close to approximation before skin sutures are inserted, if blood supply to the skin edges is excellent, a running lock stitch with cotton suture is used (Fig. 20). If blood supply is impaired somewhat, interrupted skin sutures are usually used. If skin edges do not meet, split thickness skin grafts are used to cover the defect. Drains are not inserted unless the chest wall is unusually wet or a dead space persists. The large pressure dressing is removed the 3d postoperative day, when skin flaps are adherent.

In cases so treated, skin slough has been minimal, pocket-

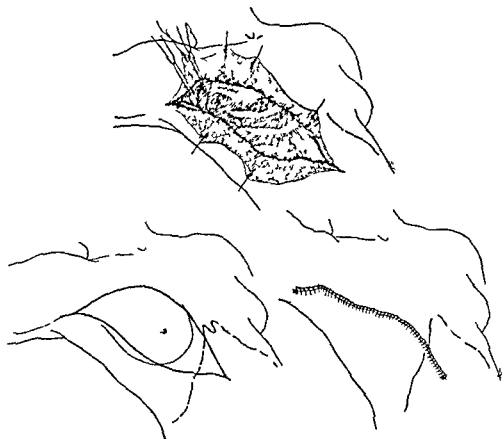


Fig 19 (top) —Many subcutaneous sutures placed in muscles and fascia to fix skin flaps in position and fill in dead spaces

Fig 20 (bottom) —Area of incision and secure fixation of skin flaps in axillary fossa and on chest wall

(Courtesy of Larsen B B JAMA 159 24 Sept 3 1955)

ing of serum or blood has been unusual and extensive early movement of the shoulder has been possible with less pain Postoperative wound inflammation has been minimal and it is believed this will decrease incidence of lymphedema of the upper extremity

Use of Plastic Prosthesis in Breast Plastic and Other Soft Tissue Surgery, with particular reference to Ivalon (poly vinyl) sponge, is reported by W John Pangman, II, and Robert M Wallace<sup>7</sup> (College of Med Evangelists)

Ivalon, a white material that looks like bread, is a polymer of polyvinyl alcohol with formaldehyde When introduced into the body fluids enter the sponge, fibroblasts and blood vessels grow into it and it acts as a framework for living tissue while its fibers remain strong but inert If the mass is cut into, it will bleed Ivalon is highly contaminable As

originally supplied, some mold spores were found that were not destroyed until three autoclavings. The present method is vacuum sterilization, followed by formaldehyde gas for several hours, then further sterilization in vacuum. To avoid sterile drainage, believed due to residual formaldehyde in the sponge, the prosthesis is boiled 30 minutes the day before operation.

Ivalon implants were used in more than 114 chins and proved far superior to bone or cartilage. The insert should be  $1\frac{1}{2}$ -2 times the thickness of corresponding bone or carti-



Fig 21 (left) —Appearance following bilateral mastectomy

Fig 22 (right) —Four months later showed ex-

palpation as a normal breast.

(Courtesy of Pangman W

August 1955)

of prosthesis. Follow  
r was as soft to deep

J Surg 63 503 512

lage to allow for compression. Ivalon has also been used successfully to build up minor depressions around the forehead and orbits. Results on dorsal nasal defects have been variable; if no infection occurred they were excellent.

Use of plain Ivalon sponge for breast plastic operations was discarded early because (1) a large percentage drained excessively even without infection and over 10% had to be removed, (2) sponges became firm to hard and were palpable as foreign bodies and (3) shrinkage was 25-75%. A compound prosthesis was then devised which overcame most of these objections.

**METHOD**—A 4 cm slit is made near the base of Ivalon sponge which has been cut and shaped to desired size, and inner portion is carefully cut away, leaving a shell about 5-8 mm thick. The segment of sponge removed is sealed airtight in a polyethylene sack and reinserted into the shell. The slit is closed using interrupted 4-0 black

silk The outer shell affords an inert framework that becomes fixed to surrounding tissue The inner sack prevents further ingrowth of fibrous tissue and acts as an inner tube to prevent collapse and also reduces fluid accumulation throughout the sponge, reducing weight and danger of drainage

Over 400 of these prostheses have been used, and since introduction of present method of sterilization, none has had to be removed because of drainage or infection Only two implants drained after 72 hours and these healed promptly Shrinkage has been 0-20% Breasts are usually firmer than normal, but not objectionable and some implants cannot be detected by palpation Figures 21 and 22 show a patient who had had bilateral semiradical mastectomy which caused severe psychic trauma Three months after insertion of the prosthesis, when the capsule on the sponge had developed, a small incision 1 cm lateral to the nipple site was made and an area 1.5 cm in diameter undermined for insertion of a piece of Ivalon sponge at the nipple site This secondary insert simulated nipple projection and areolar appearance could be achieved by tattoo

Breast prosthesis for patients who have had mastectomy for cancer is done only with recommendation or approval of the surgeon who performed the operation Subcutaneous mastectomy with immediate insertion of a prosthesis is being used increasingly in patients with benign lesions Promiscuous use of prosthesis to build up small breasts is condemned and should never be done in patients with a family history of breast cancer

Evaluation of Treatment of Cancer of the Breast at University of Edinburgh (Scotland), under Direction of Dr Robert McWhirter, 1941-47, is presented by Lauren V Ackerman<sup>8</sup> (Washington Univ) Of the 1882 patients treated 786 were living at the fifth year, 719 of this group were reviewed McWhirter's treatment, regardless of stage is simple mastectomy followed by irradiation according to his own technic Review of pathologic sections of over 90% of the cases revealed that 13 patients did not have cancer, all of whom survived without evidence of disease Most errors were in patients with intraductal papillomas Deletion of these cases (2%) does not appreciably alter the end results

The patients were staged often after simple mastectomy,

although a few were classified before. A freely movable, small lymph node in the axilla immediately placed the patient in stage 2. Error in palpation of the axilla is large, approximately 30%, and usually was made in the direction of a false negative.

Fields for irradiation were so outlined that the upper end of the humerus, clavicle, scapula and rib cage received considerable radiation, given in a short period—two weeks—all fields being treated daily. Usually there were two fields,  $25 \times 10$  cm. and two of  $15 \times 10$  cm. The combination of large fields and short periods resulted in considerable morbidity. Extensive irradiation damage, with multiple fractures of ribs, clavicle, and/or humerus, or fixation of the shoulder joint occurred in 47 patients. In three, the arm had to be amputated. Radiographically, bone changes were often misinterpreted as osteomyelitis or metastatic cancer. Most of these instances occurred in the earlier years, and changes in technic probably have reduced such morbidity.

McWhirter's statement that, with radiation, axillary lymph nodes are more easily sterilized than primary breast carcinoma (for this reason he removes the breast and then irradiates the axilla) is clinical supposition rather than pathologic fact. In several patients lymph node enlargement persisted after completion of radiation, with subsequent surgical removal enough later to judge effectiveness of therapy. In all, cancer in the lymph nodes showed no detectable radiation effect.

In patients with local persistence or distant metastases, hormone therapy of various types was given freely. At least 220 had ovarian sterilization by irradiation immediately after simple mastectomy, apparently regardless of stage of disease or age of patient, making it difficult to compare this group with a group treated only by surgery.

Local persistence rate increased by stages and was 16% in stages 1 and 2, the preferable operable stages. In many instances, lesions appeared in the irradiated field. A fairly high number died after the five years (McWhirter reported only five year survivals); 247 were either dead or dying, and 175 (stages 1 and 2) of these were in the operable group. Incidence of local persistence in those who died before the fifth year is not known.

McWhirter believes that when the axilla is dissected,



cancer is spread. This might be true in a fixed axilla with tumor growing beyond the capsule of the nodes into soft tissues. In an operable case, with the tumor in a few nodes the trained surgeon can do en bloc dissection of the axilla with little trauma and without cutting into the tumor. Ackerman thinks that McWhirter may be running a much greater risk of disseminating cancer by using simple mastectomy, particularly in locally advanced disease.

There is apparently nothing magic about McWhirter's treatment of cancer of the breast and this disease in Scotland as elsewhere, is often incurable. If anyone wishes to pursue the method, the surgeon, radiotherapist and pathologist interested in the venture must be well trained and capable. Primary treatment must not be complicated by prophylactic ovarian irradiation unless this is also standardized. All patients must be followed and there must be an attempt to prove or disprove possibility of destruction of cancer in lymph nodes.

After conclusion of the study Ackerman believes that if patients are properly selected for radical mastectomy and operated on by trained surgeons this method must yield the greatest number of permanently cured patients.

► [It is curious how fashions change in medicine as in other fields. A forceful character arises now and then with an innovation of treatment of some kind and if he has the qualities of a good salesman he may gain a considerable following of uncritical people. Probably the medical profession is as gullible as any other. At any rate the McWhirter ideas on the treatment of carcinoma of the breast were being swallowed with far too little critical appraisal. It was high time for a hard boiled review of the whole situation: the medical profession should be grateful to Dr. Ackerman for this. Those who know him could be sure that he would be frank and uninhibited in his opinions. To those who do not know him the editor will say that he is one of the outstanding surgical pathologists of the world who knows what he is talking about. We should also be grateful to Dr. McWhirter for his courtesy and innate honesty in permitting Dr. Ackerman to examine his records and cases.—Ed.]

**Surgical Treatment of Breast Cancer.** Results of Treatment at Johns Hopkins Hospital. Edward F. Lewison<sup>9</sup> cites the world wide distribution of breast cancer (Fig. 23) with no special predilection for climate, race or geographic area. In the United States 9% of the 210,000 cancer deaths in 1950 were caused by malignant lesions of the breast. In 1907 Halsted reported 232 patients treated by radical mastectomy, with additional supraclavicular neck dissection in

about 50%. Three year survival for this early period was 38%, with a "cure" rate of 32% ("cure" means patients living and well without evidence of recurrence or metastases after 5 years), five year survival was 29%, cures 24%. In a later report of 950 cases treated between 1889 and 1931, almost 22% were lost to follow-up, five year survival on

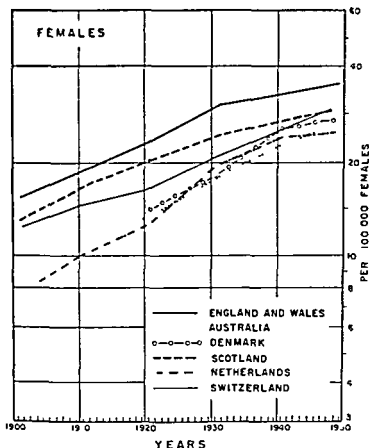


Fig 23—International trend of mortality from cancer of breast all ages (Courtesy of Lewison E F J Nat M A 47 393 398 November, 1955 from Epidemiological and Vital Statistics Report [World Health Organization 1952])

those adequately followed was only 18%. In a more recent survey of cases treated in 1932-42, five year survival (for ward patients alone) was 29%.

In the latest study (1953), long term follow-up survey of all patients with primary breast cancer treated from 1935 to 1940 showed that 204 had radical and 14 simple mastectomy. Two had local excisions (one had pulmonary metastases and the other refused treatment). Follow up of 95% showed total five year survival of 43%. Clinical cure rate was 38%. Over-all 10 year survival was 29%. Special review

cancer is spread. This might be true in a fixed axilla with tumor growing beyond the capsule of the nodes into soft tissues. In an operable case, with the tumor in a few nodes, the trained surgeon can do en bloc dissection of the axilla with little trauma and without cutting into the tumor. Ackerman thinks that McWhirter may be running a much greater risk of disseminating cancer by using simple mastectomy, particularly in locally advanced disease.

There is apparently nothing magic about McWhirter's treatment of cancer of the breast, and this disease in Scotland, as elsewhere, is often incurable. If anyone wishes to pursue the method, the surgeon, radiotherapist and pathologist interested in the venture must be well trained and capable. Primary treatment must not be complicated by prophylactic ovarian irradiation unless this is also standardized. All patients must be followed and there must be an attempt to prove or disprove possibility of destruction of cancer in lymph nodes.

After conclusion of the study, Ackerman believes that if patients are properly selected for radical mastectomy and operated on by trained surgeons, this method must yield the greatest number of permanently cured patients.

► [It is curious how fashions change in medicine as in other fields. A forceful character arises now and then with an innovation of treatment of some kind and if he has the qualities of a good salesman he may gain a considerable following of uncritical people. Probably the medical profession is as gullible as any other. At any rate the McWhirter ideas on the treatment of carcinoma of the breast were being swallowed with far too little critical appraisal. It was high time for a hard boiled review of the whole situation: the medical profession should be grateful to Dr. Ackerman for this. Those who know him could be sure that he would be frank and uninhibited in his opinions. To those who do not know him the editor will say that he is one of the outstanding surgical pathologists of the world who knows what he is talking about. We should also be grateful to Dr. McWhirter for his courtesy and innate honesty in permitting Dr. Ackerman to examine his records and cases.—Ed.]

**Surgical Treatment of Breast Cancer. Results of Treatment at Johns Hopkins Hospital.** Edward F. Lewison<sup>9</sup> cites the world wide distribution of breast cancer (Fig. 23) with no special predilection for climate, race or geographic area. In the United States, 9% of the 210,000 cancer deaths in 1950 were caused by malignant lesions of the breast. In 1907 Halsted reported 232 patients treated by radical mastectomy, with additional supraclavicular neck dissection in

about 50% Three year survival for this early period was 38%, with a "cure" rate of 32% ("cure" means patients living and well without evidence of recurrence or metastases after 5 years), five year survival was 29%, cures 24% In a later report of 950 cases treated between 1889 and 1931, almost 22% were lost to follow-up, five year survival on

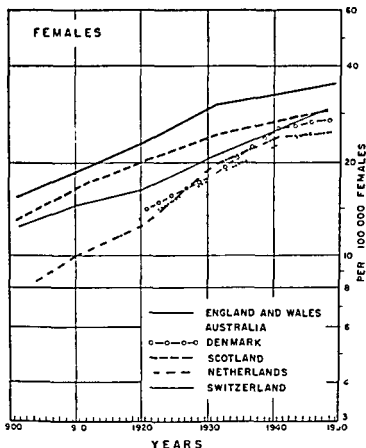


Fig 23—International trend of mortality from cancer of breast all ages (Courtesy of Lewison E F J Nat M A 47 393 398 November 1955 from Epidemiological and Vital Statistics Report [World Health Organization 1952])

those adequately followed was only 18% In a more recent survey of cases treated in 1932 42, five year survival (for ward patients alone) was 29%

In the latest study (1953), long term follow-up survey of all patients with primary breast cancer treated from 1935 to 1940 showed that 204 had radical and 14 simple mastectomy Two had local excisions (one had pulmonary metastases and the other refused treatment) Follow-up of 95% showed total five year survival of 43% Clinical cure rate was 38% Over all 10 year survival was 29% Special review

cancer is spread This might be true in a fixed axilla with tumor growing beyond the capsule of the nodes into soft tissues In an operable case, with the tumor in a few nodes, the trained surgeon can do en bloc dissection of the axilla with little trauma and without cutting into the tumor Ackerman thinks that McWhirter may be running a much greater risk of disseminating cancer by using simple mastectomy, particularly in locally advanced disease

There is apparently nothing magic about McWhirter's treatment of cancer of the breast, and this disease in Scotland, as elsewhere, is often incurable If anyone wishes to pursue the method, the surgeon radiotherapist and pathologist interested in the venture must be well trained and capable Primary treatment must not be complicated by prophylactic ovarian irradiation unless this is also standardized All patients must be followed and there must be an attempt to prove or disprove possibility of destruction of cancer in lymph nodes

After conclusion of the study, Ackerman believes that if patients are properly selected for radical mastectomy and operated on by trained surgeons, this method must yield the greatest number of permanently cured patients

► [It is curious how fashions change in medicine as in other fields A forceful character arises now and then with an innovation of treatment of some kind and if he has the qualities of a good salesman he may gain a considerable following of uncritical people Probably the medical profession is as gullible as any other At any rate the McWhirter ideas on the treatment of carcinoma of the breast were being swallowed with far too little critical appraisal It was high time for a hard boiled review of the whole situation the medical profession should be grateful to Dr Ackerman for this Those who know him could be sure that he would be frank and uninhibited in his opinions To those who do not know him the editor will say that he is one of the outstanding surgical pathologists of the world who knows what he is talking about We should also be grateful to Dr McWhirter for his courtesy and innate honesty in permitting Dr Ackerman to examine his records and cases—Ed]

**Surgical Treatment of Breast Cancer Results of Treatment at Johns Hopkins Hospital** Edward F Lewison<sup>9</sup> cites the world wide distribution of breast cancer (Fig 23) with no special predilection for climate race or geographic area In the United States 9% of the 210 000 cancer deaths in 1950 were caused by malignant lesions of the breast In 1907 Halsted reported 232 patients treated by radical mastectomy, with additional supraclavicular neck dissection in

about 50%. Three year survival for this early period was 38%, with a "cure" rate of 32% ("cure" means patients living and well without evidence of recurrence or metastases after 5 years), five year survival was 29%, cures 24%. In a later report of 950 cases treated between 1889 and 1931, almost 22% were lost to follow-up, five year survival on

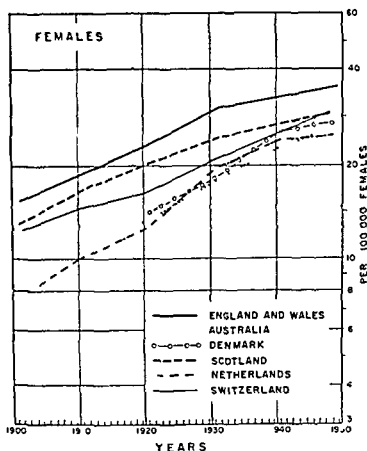


Fig. 23—International trend of mortality from cancer of breast all ages (Courtesy of Lewison E. F. J. Nat. M. A. 47:393-398 November 1955 from Epidemiological and Vital Statistics Report [World Health Organization 1952])

those adequately followed was only 18%. In a more recent survey of cases treated in 1932-42, five year survival (for ward patients alone) was 29%.

In the latest study (1953), long term follow up survey of all patients with primary breast cancer treated from 1935 to 1940 showed that 204 had radical and 14 simple mastectomy. Two had local excisions (one had pulmonary metastases and the other refused treatment). Follow-up of 95% showed total five-year survival of 43%. Clinical cure rate was 38%. Over all 10 year survival was 29%. Special review

of 64 cases with 10 year survival or longer failed to reveal any histologic characteristic that could be correlated with a long survival. A comparatively poor prognosis for young women with breast cancer was demonstrated, in that five year survival was only 30% among patients under age 40.

Until realization of hopes for more successful treatment of cancer of the breast, fundamental principles of radical mastectomy must not be abandoned as untenable in favor of either more conservative or more formidable procedures. Despite progressive and commendable clinical experiments with newer therapeutic technics, e.g., McWhirter's method, and more radical resections as practiced by Dahl-Iverson, Urban and Wangenstein, the classic Halsted radical mastectomy sets a high standard of surgical treatment. Lewison believes it still remains the operation of choice for most cases of breast cancer.

► [This report of results accomplished by the Halsted Willy Meyer principles of treating carcinoma of the breast is a fitting complement to the preceding article by Ackerman on the shortcomings of McWhirter's ideas of treatment. Anybody who knows the facts can hardly deny that the principle of the radical mastectomy operation should not yet be abandoned—Ed.]

**Limitations in Diagnosis and Treatment of Breast and Other Cancers. A Review.** According to N. E. McKinnon<sup>1</sup> (Univ. of Toronto), aggressive programs over the past 25-30 years for control of cancer mortality, and particularly that of breast cancer, have failed to make any impression on the later recorded mortality, an indication that remote spread occurs before the lesion can be diagnosed and treated. Evidence shows that "stage I" does not mean short duration but suggests the type of breast cancer. Microscopy does not reveal accurately the biologic characteristics—metastatic or lethal propensity—of a tumor. "Proved microscopically" does not necessarily signify a progressive lethal cancer but an architecture similar to or identical with that of progressive lethal cancer. Nonprogressive lesions, unavoidably included as lethal cancer, make up a large part of most stage I cancers, whether the latter form a large or small part of a series. Wide variations in survival of patients with cancers of other stages also reflect wide variations in malignancy in these stages that are not accurately revealed by microscopy.

(1) Canad. M. A. J. 73:614-624, Oct. 15, 1955.

Evidence that treatment of breast cancer prevents death in a considerable proportion of cases or that early treatment is greatly superior in this regard must be rejected because it is based mostly on survival rates in series of cases whose comparability was, in many instances, patently lacking and, in all, incapable of proof through microscopy. Differences in survival are reasonably attributable to differences in type of case rather than to differences in time or type of treatment. Failure to take into account the present inability to differentiate accurately, through microscopy, between non-lethal and lethal cancers and between different degrees of malignancy in lethal cancer explains many inconsistencies and contradictions in breast cancer reports.

Findings from critical clinical analyses conform with the hypothesis from the level trends in vital statistics of breast cancer. The value of local treatment cannot, therefore, be measured in lives saved, but must be in the physical and mental relief provided. Evidence fails to give assurance that material reduction of deaths from any metastasizing cancer has been achieved. High survivals reported for early treatment of cervical cancer and the like are attributable to misconceptions and present insuperable difficulties in diagnosis and differentiation similar to those found in regard to breast cancer. In metastasizing cancers that kill through local extension and its complications before remote metastases cause trouble, adequate local treatment can postpone death. In nonmetastasizing cancers, such as most skin cancers or what are called cancers, local treatment can cure, but these account for only a small part of cancer mortality.

As cancer data are unavoidably inaccurate, the possibility that death may be prevented in an occasional case of breast or other metastasizing cancer by early or extensive treatment cannot be denied, but, if any, such cases are too few to make a decisive impression on recorded mortality.

► [This startling article by McKinnon will certainly astonish many surgeons. Can it be true that despite all the effort put into the problem of the treatment of breast cancer no impression has been made on the recorded mortality? Undoubtedly many will refuse to believe the conclusions he draws. One can hardly attribute the failure to get better results to a poor quality of surgery since probably in general the actual surgery performed on patients with this disease has been better during the past 25 years than at any time previously because of the better training of surgeons now. It is unfortunate that we do not have space to reprint the whole article because all of it should be read.—Ed.]



**Significance of Parasternal Glands (So called Mammary Glands) in Spread and Prognosis of Carcinoma of the Breast** is discussed by E. Kaiser<sup>2</sup> (Zurich) Since the summer of 1954, he has removed these glands during radical operation for breast carcinoma in 40 patients In nine (23%), mammary glands showed carcinoma Mammary metastases were present in 2 of 11 medially situated tumors and in 7 of 29 lateral growths The inadequacy of preoperative diagnosis was demonstrated In one case, axillary glands were tumor free, contrary to expectations, and in another instance, both axillary and parasternal glands were involved, although the tumor was thought to be benign Involvement of parasternal glands escapes preoperative detection

The relatively high percentage of diseased parasternal glands imposes the obligation to remove these glands at operation for breast cancer, regardless of irradiation before or after operation, or both Since there is uncertainty whether x-rays can actually sterilize axillary glands they certainly cannot be relied on to destroy all cancer in the much deeper parasternal glands, which are partially covered by costal cartilage The surgical technic is easy, if intra tracheal anesthesia is used to avoid danger from opening the pleura This occurred accidentally four times in these 40 cases

**TECHNIC**—Removal of mammary glands lengthens radical breast operation by only 10-20 minutes En bloc dissection of the breast the sternocostal two thirds of the pectoralis major and entire axillary fatty tissue and glands is carried out The medial skin edge and insertion of the pectoralis major are dissected back toward the sternum The cartilage of ribs 2-3 and sometimes 4 is removed The branch of the internal mammary artery can be clamped temporarily but often it is preferable to allow some blood loss and to strive for rapid ligation This vessel is easily identified if it is remembered that it may lie under the sternum and as much as 2.5 cm. to the side It overlies endothoracic fascia and pleura The pleural envelope can usually be avoided but in case it is torn it can be mobilized and sutured With intratracheal anesthesia however suture is not necessary The whole mammary cord is resected for about 8 cm Small glandules are found along this vessel that are not macroscopically recognizable The insertion of the pectoralis major is drawn over the site of removed cartilage sutured to intercostal musculature an axillary drain is inserted and closure is made in layers

In all cases the postoperative course was uneventful

Loss of cartilage is palpable after operation, but this is neither troublesome to the patient nor visible

Statistics from the University of California demonstrated that if patients with breast carcinoma came to operation within one month after appearance of the first symptom, 48% had mammary gland involvement. Of those without such metastases, 60% had five year cures, compared with 40% in the total group. Since modern intratracheal anesthesia has eliminated danger of pneumothorax during operation, removal of parasternal glands should become an integral part of every operation for breast carcinoma.

**Hereditary Factor in Cancer of the Breast** seems evident in cases occurring in two sisters and their half sister, reported by William V. Watt (Boston) and Hugh H. Trout, Jr.<sup>3</sup> (Roanoke, Va.). Malignant tumor was found at first

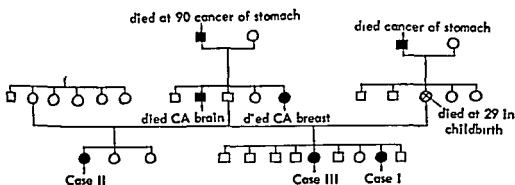


Fig. 24 — (Courtesy of Watt W. V. and Trout H. H. Jr. *Am. J. Surg.* 90:434-436, September, 1955)

operation in the full sisters aged 26 and 31, and later both had metastases, one in a vertebra and the other in a contralateral axillary lymph node.

The half-sister, 19, had lumps in the breast which were found to be benign pericanalicular fibroadenomas. About 1½ years later, fibrosis beneath the scar became indurated and a nodule was palpable in the axilla. The lesion was excised and found to be malignant, so radical mastectomy was performed. Subsequent treatment consisted of bilateral salpingo-oophorectomy, skin grafting and deep x-ray therapy. She appeared in good health, without recurrence, 15 months later. The parent common to all three patients was the father and most other cases of cancer in the family occurred on his side (Fig. 24).

Experiences with Hypophysectomy in Breast Cancer and in Diabetic Kimmelstiel-Wilson Syndrome are reported by R Luft and H Olivecrona<sup>4</sup> (Stockholm) Among 50 patients with advanced metastatic breast carcinoma, there were three postoperative deaths, one due to pulmonary embolism, one to inhalation pneumonia (in a patient with paralyzed throat muscles resulting from metastases at the base of the skull) and one to thyrotoxic crisis Three other patients died of intercurrent disease, one a few weeks after discharge, and the others, who had satisfactory remissions, six and nine months later There was no improvement in 26, all of whom died of progressive carcinoma, usually within a few months, although some lived one to two years Even in the unfavorable cases pain was decreased

Subjective and objective improvement followed hypophysectomy in 20 patients Carcinomatous ulcers and cutaneous and lymph node infiltrations disappeared or were decreased and lung and bone metastases were decreased or arrested, with no new metastases for at least six months The patients gained weight, had less pain and could, in most cases, resume work Seven in this group died after an average of 2 years, 11 were alive 1-3½ years Three patients who had had previous adrenalectomy died of progressive carcinoma a few weeks after hypophysectomy was performed

A favorable and fairly durable remission apparently can be obtained by hypophysectomy in one third to one half of cases of advanced metastatic breast carcinoma Probable effect of hypophysectomy could not be predicted by previous hormonal treatment In those who react favorably to hormone implantation, hypophysectomy yields a much more intense and lasting effect, but some patients who have little reaction to hormones may experience a good remission after hypophysectomy In the authors' experience, women over 60 and those with liver and brain metastases apparently do not respond to removal of the pituitary Before operation, no substitution therapy was administered and immediately after operation cortisone was given only as required in patients with fever On discharge, 25 mg cortisone and 100 µg thyroxin were prescribed With this substitution patients felt well and were able to work if they were not invalidated for other reasons

(4) Schweiz med Wchnschr 86 113 117 Feb 4 1956

Hypophysectomy was performed on 20 diabetics with severe vascular complications, i.e., advanced retinopathy and various degrees of kidney damage. There were three postoperative deaths (15%). Four patients died later, one apparently of hypoglycemia and one of rapidly progressive arteriosclerosis, particularly of the brain, one died in hypertensive crisis and one of uremia. In these last two, use of desoxycorticosterone instead of cortisone possibly contributed to progression of hypertension and kidney failure, although both patients were in poor condition before operation. Nevertheless, use of desoxycorticosterone has been abandoned.

Twelve patients were living three months to four years later. Functional tests showed that hypophysectomy was complete in all but one. Final substitution therapy consisted of 10-15 mg cortisone, 100-150  $\mu$ g thyroxin, testosterone in men and occasionally estrogen in women. Insulin need decreased after operation to a third or a fourth the preoperative dose, and usually stabilized at 8-24 units. Epileptic seizures refractory to the usual drug treatment occurred as a postoperative complication in some of these patients (but not in patients with carcinoma). These attacks began usually about a week after operation and disappeared by the end of the second week, although occasionally they lasted longer. The seizures were attributed principally to brain edema, which apparently is more severe after surgery in diabetics than in patients with normal cerebral vessels. Some other factor may also be present.

Decrease in systolic pressure was observed in all patients during the first year, but in two (who received desoxycorticosterone for a considerable period) followed for 25 and 43 months blood pressure again reached the preoperative level. There was a significant decrease in heart size. Roentgenologically visible calcification of peripheral arteries remained unchanged but new calcification did not appear. Most had decreased albuminuria. Blood flow through the kidney, measured by para aminohippuric acid clearance, was unchanged after operation. Conversely, glomerular filtration measured with insulin (regardless of hormonal substitution), was less than before operation, with consequent decrease in the filtration fraction. This change is related to removal of the anterior hypophysial lobe, as it was seen in

carcinoma patients with no kidney damage. Since kidney flow was unchanged, decrease in glomerular filtration may signify decreased tonus of glomerular capillaries which should influence kidney circulation favorably.

After hypophysectomy, no progression of circulatory and renal damage was evident, but whether kidney function was definitely improved is not yet certain. All patients had progressive retinopathy, visual acuity improved in seven, was unchanged in four and decreased in one. Eye grounds could be studied in 10 patients, another 2 had cataract. One patient who had progressive visual loss improved initially but definite vascular deterioration followed an exacerbation of chronic polyarthritis treated by increased cortisone administration. In nine there was no progression of retinal changes except for some new vessels in regions of abundant vascular neoplasms present preoperatively. In five, adventitious vessels regressed.

► [These authors were the pioneers in applying the operation of hypophysectomy to the treatment of advanced inoperable carcinoma of the breast. Something seems to be wrong about the arithmetic of their cases but there is no doubt that in some cases hypophysectomy is a palliative procedure. In this connection see the following three abstracts of articles by Pearson—Ed.]

**Management of Metastatic Mammary Cancer.** Olof H Pearson, Min C Li, John P Maclean, Mortimer B Lipsett and Charles D West<sup>5</sup> (Memorial Hosp., New York) state that in most women with primary breast cancer dissemination develops eventually despite mastectomy and prophylactic radiation therapy. The progression of metastatic disease is variable. The growth of mammary cancer in many cases depends on circulating hormones secreted from the ovaries, adrenals and pituitary gland. Removing or lowering the titer of these hormones results in temporary cessation of growth and regression of the cancer. All forms of endocrine therapy produce only temporary palliation. Endocrine therapy, whether by ablation or by hormone administration, has the advantage over roentgen therapy that its favorable effects are not confined to the area treated.

Oophorectomy induces objective remissions in about 44% of premenopausal women with metastatic breast cancer and is the best initial treatment for such women. The average remission period is nine months. No practical means for se-

lecting patients for oophorectomy has been found. Bilateral adrenalectomy produced objective remissions in 45% of 38 women with previous oophorectomy. The average duration of remissions was nine months. Patients who have benefited from castration are likely to benefit from adrenalectomy. Combined oophorectomy and adrenalectomy produced objective remissions in 16 of 25 postmenopausal women for an average of eight months or more and is thus the recommended initial therapy for these women. There is no practical method of selecting women for these procedures.

Total hypophysectomy produced remission in 54% of 37 cases that could be evaluated. Further time is necessary to determine the duration of remissions with this treatment.

Androgen therapy induces objective improvement in about 23% of women of all ages with breast cancer for an average of 7½ months. The mechanism of action may be that androgens neutralize the effects of endogenous estrogen. Androgen therapy should be reserved for patients with relapse after oophorectomy, adrenalectomy or hypophysectomy and for those who cannot tolerate or refuse ablative therapy. Estrogens induced objective remissions in about 44% of postmenopausal women for an average of eight months. Since they can also accelerate the growth of breast cancer, they should be used only in patients who fail to respond to castration or adrenalectomy and castration.

Cortisone in doses of 200-400 mg daily induces objective remissions in about 30% of patients with metastatic breast cancer for an average of three months, regardless of whether the tumor is estrogen dependent or not. The hormone should be reserved for patients who fail to respond to, or have a relapse after, other endocrine therapy.

► [This and the following two papers inspired by Dr. Pearson give the conclusions drawn from his extensive experience in endocrine therapy of cancer of the breast. The recent addition of hypophysectomy has given some strikingly good palliative results in some cases but not such good results in others. Dr. Pearson's approach to the use of this procedure is conservative and praiseworthy. We shall have to wait for much more experience before arriving at definite conclusions.—Ed.]

**Androgen Induced Exacerbation of Breast Cancer Measured by Calcium Excretion. Conversion of Androgen to Estrogen as Possible Underlying Mechanism.** Responses to administration of androgens and estrogens were studied by W. P. Laird, Myers, Charles D. West, Olof H. Pearson and

David A Karnofsky<sup>6</sup> (New York) in four women with breast cancer and skeletal metastases. All had undergone previous radical mastectomies, and two had had castration and x-ray therapy. None had undergone adrenalectomy. All women were premenopausal at onset of the disease, which varied in duration from 17 to 68 months. In three, clinically detectable disease was confined to the skeleton, one also had pulmonary metastases.

On the basis of the idea that active growth of tumor in bone results in liberation of calcium secondary to increased osteolysis, responses of the tumor to androgens and estrogens were measured by changes in the level of serum calcium and in calcium excretion, determined before, during and after therapeutic trials. Urinary calcium excretion of 150 mg/day or more was regarded as abnormal, since dietary intake of calcium was restricted to 200 mg/day or less. Serum calcium values of 9.2-10.8 mg/100 ml were regarded as normal. Hypercalcemia and hypercalciuria developed after administration of both hormones, and urinary calcium measurements proved to be an excellent guide to impending hypercalcemia.

It is postulated that conversion of androgen to estrogen in women may be a possible mechanism underlying androgen exacerbation of human mammary cancer. Another possible explanation for androgen exacerbation of breast cancer is that androgens may directly stimulate mammary cancer. An abnormal breast cancer cell may in some instances have lost its ability to distinguish between androgen and estrogen and thus might thrive on any gonadal steroid. Androgen exacerbation of human mammary cancer requires further study.

**Hypophysectomy in Treatment of Advanced Cancer** is reported by O H Pearson, B S Ray, C C Harrold, C D West, M C Li, J P MacLean and M B Lipsett<sup>7</sup> (New York). The rationale for this study was based on the concept that the growth of certain neoplasms might be dependent on pituitary hormones. Results were evaluated on presence or absence of regression or cessation of tumor growth. Effects could not be evaluated in 24 patients be-

(6) JAMA 161:127-131, May 12, 1956

(7) Tr A Am Physicians 68:101-111, 1955

cause of operative death (11), incomplete hypophysectomy (9) and death from cancer too soon after operation (4). Of the other 55 patients, 22 had objective remission, 31 showed no response and 2 were operated on too recently for results to be evaluated. Of the patients with remission, 21 had breast cancer; 20 others with this type failed to respond. One patient with prostatic cancer had objective remission; three did not respond. No remission occurred in choriocarcinoma, malignant melanoma, thyroid carcinoma, reticulum cell sarcoma, ovarian carcinoma and hypernephroma. Only one in seven patients with these carcinoma types were operated on.

Neither right temporal craniotomy (16) nor trans-sphenoidal hypophysectomy (10) proved satisfactory technically for operation. Right frontal craniotomy, with direct visualization of the hypophyseal stalk between the optic nerves, was done in 53 patients. Lumbar cerebrospinal fluid drainage helped exposure. The gland was removed piecemeal through enlargement of the hole in the diaphragma sellae left when the stalk was coagulated and divided. Zenker's fluid was irrigated into a sponge filling the sellar cavity to kill residual cells. Three patients died, three had minor visual field defects, two had bitemporal hemianopsia (one with nearly complete loss of vision in left eye), one had transient hemiplegia and one had third nerve paresis. Three had incomplete hypophysectomy, as judged by development of myxedema within four to eight weeks, adrenal insufficiency when cortisone or ACTH was withdrawn and disappearance of gonadotropins from the urine.

Hypophysectomy induced remissions in some women with breast cancer with relapse after oophorectomy and adrenalectomy, supporting the concept that a pituitary factor may be needed for tumor growth in such cancer. This procedure may possibly produce a summation of beneficial effects of oophorectomy, adrenalectomy and hypophysectomy performed in sequence. No satisfactory method of selecting patients for hypophysectomy has been devised. Failure to respond to androgen or estrogen therapy does not mean that the patient may not respond to hypophysectomy.



**Endocrine Insufficiency after Hypophysectomy in Patients with cancer of the breast and of the prostate and with diabetes mellitus** was studied by R Luft, H Olivecrona U von Euler, D Ikkos, H Ljunggren, L B Nilsson J Sekkenes, B Sjogren and H J Waschewsky<sup>s</sup> (Serafimer Hosp, Stockholm)

*Thyroid function*—In patients with no thyroid substitution, BMR fell during the third to fourth week after operation to  $-20\%$  and remained at this level. Administration of  $100\text{ }\mu\text{g}$  thyroxin daily caused little increase in BMR even when subjective symptoms of hypothyroidism seemed to be alleviated. In 12 or 16 patients, uptake of  $\text{I}^{131}$  and 24 hour output in urine were low, in 2, low normal, and in 2, normal. Cholesterol levels in plasma (in nondiabetic patients) generally remained at preoperative level, whether or not thyroid was given.

*Adrenocortical function*—Excretion of 17-ketosteroids during the second week after operation usually was less than  $2\text{ mg/day}$  and remained at this level. Serial studies in some patients showed definite reduction by the end of the first week. With  $25\text{ mg}$  cortisone/day, excretion in about half the patients was over  $2\text{ mg/day}$ . This agrees with previous studies showing that cortisone is partially metabolized to 17-ketosteroids. In all hypophysectomized patients, decrease of eosinophils four hours after receiving  $25\text{ mg}$  ACTH was less than the normal  $40\%$ , a sign of cortical insufficiency. Decrease in eosinophils four hours after  $0.3\text{ mg}$  epinephrine was under  $40\%$  in  $90\%$  of patients not receiving cortisone. Results of the epinephrine test were normal in over half the patients receiving  $10\text{--}25\text{ mg}$  cortisone. This shows that epinephrine can cause decrease in circulating eosinophils only in presence of cortisone and not by direct or indirect stimulation of the adrenal cortex. Results of administration of  $0.1\text{ unit/kg}$  body weight intravenously in patients with carcinoma after hypophysectomy compared, with 30 overloading tests in 24 healthy controls showed that there was no difference between patients receiving  $25\text{ mg}$  cortisone daily and those without substitution, that blood sugar in hypophysectomized patients during the entire period of overloading lay below normal, that fasting blood sugar in hypophysectomized patients was lower (hence not

directly comparable with that in normals), that the percentile blood sugar decrease from the fasting value in normal and hypophysectomized patients is the same, after 180 minutes, amounting to 95% clearance, although clearance in hypophysectomized patients was slower before this. Within four hours after taking 1 L. water, little increase of diuresis or decrease of specific gravity was noted in hypophysectomized patients. With cortisone, results of the water test were normal.

*Adrenal medullary function*—No obvious change in urinary excretion of epinephrine and nor epinephrine occurred, except during the first two weeks after operation when a slight increase was noted.

*Water balance*—Course of diuresis during the first month after operation was always similar, whether the patient received ACTH or cortisone the whole time, only during the first postoperative days or not at all. The only difference was that polyuria disappeared in patients who received no cortisone, after the fourth postoperative week. If cortisone was given polyuria was produced. During the later course, polyuria disappeared in all patients, even when cortisone was given continually.

The authors conclude that, after hypophysectomy, thyroid and adrenal cortical insufficiency are permanent, that function of the adrenal medulla apparently remains intact and that transitory diabetes insipidus develops but finally disappears.

**Fundamental Concepts Determining a Philosophy of Treatment in Mammary Carcinoma.** A Review is presented by Norman C. Delarue<sup>9</sup> (Toronto Gen'l Hosp.), who emphasizes the fact that changes are almost certain in any therapeutic regimen as knowledge increases and its effectiveness is critically appraised.

A simplification of the five stage classification is suggested, in which the first two stages are grouped together, and stages III and IV considered as a unit representing locally advanced disease. The fifth or final stage, i.e., with accompanying metastases, represents a separate problem. Stages I and II are treated identically as far as excision is concerned. With outer quadrant involvement in which metastases to the internal mammary chain are relatively

(9) *Canad. M. A. J.* 73:597-614 Oct. 15, 1955.



must be excised. Simple mastectomy would be the most acceptable alternative, except that radiotherapy should be preoperative rather than postoperative.

When distant metastases are present, treatment of the local lesion is purely palliative, although it has physical as well as psychologic value, particularly when an extensive local lesion, possibly complicated by ulceration and secondary infection, is producing deleterious general effects. Simple mastectomy is usually performed, with local radiotherapy preoperatively dependent on extent of local lesion.

Established methods of irradiation are still the most effective for metastases involving the skin of the chest wall, osseous system and accessible lymph nodes. In large pleural effusions and ascitic collections requiring frequent aspirations, instillation of radioactive gold affords valuable palliation. In lesions not suitable for irradiation, agents affecting the disseminated lesions via the blood stream must be resorted to.

Because estrogen deprivation is more effective than androgen administration in arresting growth of the neoplasm, surgical castration should be the first step in premenopausal patients, and adrenalectomy should be considered when reactivation of metastases appears. In older women, androgenic therapy is favored since estrogen deprivation implies simultaneous oophorectomy and adrenalectomy. If testosterone is ineffective or loses its value, estrogen treatment may be attempted with caution. Later, adrenalectomy may be advisable in patients with disease of long duration, metastases involving bone and superficial soft tissues and preferably a favorable response to irradiation. Only when patients are willing to accept a gamble is this procedure otherwise considered.

After estrogen deprivation androgenic therapy may still be tried. Large doses of cortisone or pharmacologic dosage of estrogens (preferably in postmenopausal women only) may be attempted. Hypophysectomy now is restricted to patients who favor further major surgery after previous therapy has failed. The important feature of this procedure is determination of its potentiality to equal combined results of estrogen deprivation, androgenic therapy and attempts at pituitary depression with cortisone and estrogens. Immunologic control and use of metabolic antagonists require

further investigation and provide hope for eventual discovery of more effective therapy

Emphasis is laid on the necessity for tempering surgical daring with mature philosophic judgment in decisions regarding treatment, particularly for the patient with metastases. Palliation must relieve suffering and restore function, with reasonable expectation of adequate increase in survival.

Treatment of Carcinoma of Breast in the Aged is discussed by Thomas C. Case<sup>1</sup> (Goldwater Mem'l Hosp., New York). In 1943, it was reported that 10% of breast cancers occurred in patients 70 or over. Byrd reported 11.3% in the advanced age group. In the author's series, 33% were over 60 and about 10% over 70. This group requires more attention, particularly since in some surgical centers as many as a third of the patients of advanced age are not treated surgically, mostly because they are considered too old or to have inoperable tumor.

Lesions observed most often in the aged are of the slow growing, atrophic scirrhous type, or the medullary type with lymphoid infiltration that eventually ulcerates after a long history of tumefaction. Since neoplastic cells find little nourishment in a tumor bed not conducive to prolific and rapid growth, it would seem that extensive surgical procedures should never be considered for therapy. There is also growing awareness that microscopically diagnosed carcinoma need not be relentlessly progressive autonomous growth but that cyclic remissions and exacerbations or even spontaneous arrests may occur. This is even more true in the aged. Removal of the primary focus together with the breast and accessible axillary nodes therefore seems sufficient. If fear of disseminated cancer cells should exist, radiation therapy can be applied effectively.

The surgeon's aim should be not only to cure the patient but also and principally, to prolong life and increase physical and mental comfort. In view of the actual life expectancy, it is no compromise to select simpler procedures for older patients. That radical procedures can be performed without undue mortality, however, does not justify their indiscriminate use when more conservative measures would be equally successful in properly selected cases.

(1) J. Am. Geriatrics Soc. 4:292-295, March 1956.

Definitive treatment depends on the stage of the disease and condition of the patient. Cancers considered inoperable, either because of advanced stage of the disease or other constitutional disorders, should be treated with radiation, which is usually beneficial and often amazingly effective. Hormonal therapy also has its place in palliation in advanced cases.

Re-examination of Problem of Castration for Carcinoma of Breast is presented by L. Schonbauer and E. Schmidt-Ueberreiter<sup>2</sup> (Univ. of Vienna), with comparison of results with and without such treatment. Of 63 premenopausal patients in whom ovarian function was not disturbed, 51 died within five years, 37, or over half, within the first two years after breast operation. Of 17 patients in whom the ovaries were removed prophylactically immediately after breast resection, with follow-ups of one year nine months to five years five months (13 over two years), 14 were in good condition, with no evidence of progression of carcinoma, 2 had bone metastases and 1 was dead.

Of 205 patients with satisfactory data on menstrual status, operated on for breast cancer from 1941 to 1951, with follow-up of at least three years, 101 were still living. Only 16 survivors had active ovarian function contrasted with 85 without ovarian function. These findings not only justify prophylactic castration but demand it.

The authors recommend preliminary blocking of the anterior pituitary with androgenic hormones, as advocated by Schmaus. As soon as diagnosis of breast cancer is made 50 mg. male hormone is given every second day during preoperative roentgen radiation of the tumor. Increasing experience with breast cancer has brought conviction that combined treatment—preoperative blocking of anterior pituitary, preoperative radiation of the tumor, radical operation, castration and postoperative androgen treatment for varying periods—offers the most to the patient.

**Inflammatory Carcinoma of Breast: A Critique of Therapy** C. S. Rogers and W. T. Fitts, Jr.<sup>3</sup> (Univ. of Penn.) state that of 1,774 patients with pathologically proved carcinoma of the breast, 46 (2.6%) had primary inflammatory carcinoma of the breast. All had erythema, edema, peau

(2) Wien klin. Wchnschr. 67:847-849, Oct. 28, 1955.

(3) Surgery 39:367-370, February, 1956.

d'orange and increased local heat. There were 45 women and 1 man, average age 49.9, of whom 14 were Negro. Half the women were postmenopausal. Cancer of both breasts was found initially or occurred later in 30%, 15% had a nipple discharge, 95% had axillary metastases, and 43% had supraclavicular metastases at the time of initial examination.

The methods of treatment were: x-ray radiation in 24, radical mastectomy, 10, simple mastectomy, 10, estrogen therapy, 1, and no therapy, 1. With one exception, all patients who had a radical mastectomy received postoperative irradiation, and all but one of the patients who had a simple mastectomy received postoperative irradiation. One of the patients who had a radical mastectomy and five who had a simple mastectomy were given preoperative irradiation. No patient received hormones in the terminal stages of the disease.

One patient was alive and free of disease eight years after radical mastectomy. Another patient, treated by x-ray irradiation alone, was alive seven years after the beginning of treatment but both breasts and a large portion of the anterior chest wall were involved with cancer, although no distant metastases were demonstrable. All the other patients were dead. There was a 60% mortality in the first year, 80% within two years and over 90% within three years. One third of those treated primarily with irradiation died within six months or less. One death occurred in the group with radical mastectomy, and one in the group with simple mastectomy, within six months. No matter what form of treatment was used, the survival rate was poor.

The best means of treating inflammatory carcinoma of the breast is unknown. The disease runs a rapidly fatal course regardless of the type of therapy. There is no evidence, however, that surgical intervention accelerates the course, nor are data available in the literature that show significantly better results following palliative measures. The widespread teaching that operation is contraindicated in all patients with inflammatory carcinoma of the breast is untenable.

## THE LUNGS AND PLEURA

**Lobar Ventilation and Oxygen Uptake in Man: Influence of Body Position.** Stig Borje Mattson and Eric Carlens<sup>4</sup> (Uttran, Sweden) investigated spirometrically the ventilation and oxygen uptake in the upper lobe and the basal lobes of the right lung in seven men with tuberculosis of the left lung. The study was to determine if and to what extent any shift occurs in the blood flow between the two regions of the lesser circulation above and below the pulmonary trunk when position is changed from recumbent to erect. The right lung is well adapted to such a study since, in the erect subject, the upper lobe is almost entirely above the level of the pulmonary trunk, and the two basal lobes are below. The right lung showed no pathology in any of the patients. None had cardiac disease, and normal pressure existed in the lesser circulation.

One catheter was placed in the right upper lobe bronchus and another in the bronchus leading to the middle and lower lobes. Comparative study showed an inconsiderable average decrease in ventilation ( $m = 16$ ) but an appreciable average decrease in the oxygen uptake ( $m = 186$ ) in the upper lobe with a change from the supine to the erect position. The greatly decreased perfusion, probably orthostatic in origin, with practically unaltered ventilation of the upper lobe in the erect position should lead to an increase in the alveolar oxygen tension. The results of the study support the old theory that the changed circulation in the apexes of the lungs comprises a phthisiogenetic factor. The increased oxygen tension in the tissues may produce more favorable growth conditions for tubercle bacilli. It is justifiable to assume that the venous blood flow in the apical parts is even less and perhaps in certain cases, even totally absent. It is improbable that the capillaries collapse.

**Pulmonary Ventilation during Open Thoracotomy: Inflation and Deflation Time Ratios and Pressures.** Thomas F. Nealon, Jr., George J. Haupt, Joyce E. Price and John H. Gibbon, Jr.<sup>5</sup> (Jefferson Med. Center, Philadelphia) state

(4) J. Thoracic Surg. 30: 676-682, December 1955.

(5) Ibid., pp. 665-675.



that respiratory acidosis is a common occurrence in operative procedures and difficulty in achieving adequate pulmonary ventilation is increased when the thoracic cavity is opened. Manual or mechanical compression of the rebreathing bag, providing intermittent positive pressure, has been used to improve ventilation during surgery. There is evidence that intermittent positive and negative pressure ventilation is more effective in preventing respiratory acidosis than manual or mechanical compression. A study was made of the effect on pulmonary ventilation of the relative duration of inflation and deflation and of the pressures employed in 21 operations involving open thoracotomy in 20 patients.

With open thoracotomy, the degree of expansion of the lung is a function of the mean endotracheal pressure within the obvious limits of collapse and overdistention. In the absence of generalized pulmonary disease, a mean endotracheal pressure of  $+4$  to  $+6$  cm H<sub>2</sub>O resulted in normal expansion of the lungs. With emphysema, lower mean pressures were required to avoid overexpansion of the lungs. Avoiding collapse or distention of the lungs, with a respiratory rate of 20/minute, and with a constant difference in pressure between inflation and deflation, the greatest pulmonary ventilation was achieved when duration of inflation was equal to duration of deflation.

Avoiding collapse or distention of the lung, with a respiratory rate of 20/minute, and with equal duration of inflation and deflation, the pulmonary ventilation varied directly with the difference in pressure between inflation and deflation. Greater pulmonary ventilation at a lower mean pressure can be achieved with the use of negative pressure during deflation. Negative pressure is also of great value in assisting the deflation of emphysematous lungs. The use of positive and negative pressure ventilation resulted in normal or reduced levels of  $P_{CO_2}$  of arterial blood in 16 of 18 cases of open thoracotomy.

**Lobar Alveolar Gas Concentration after Pneumonectomy** was studied by C. J. Martin, Frank Cline, Jr. and Helen Marshall<sup>6</sup> (Univ. of Washington) in the remaining lung (four right one left) of five patients. Oxygen concentration was significantly higher in the upper than the lower lobe (mean 1.49 vol %). Carbon dioxide was lower in the upper

lobe by 0.71 vol % Mean difference between lobes, higher in the upper lobe, in the respiratory exchange ratio was 0.06 (normal, 0.17) For the supine position, oxygen concentration was lower in the upper lobe (mean, 0.53 vol %) Carbon dioxide was lower in the upper lobe (mean, 0.31 vol %) Respiratory quotient (RQ) was lower in upper lobe by 0.14 Nitrogen indexes were high for patients with total ventilation in one lung, and residual air/total capacity ratios were moderately elevated, indicating pulmonary distention

When erect, the patient with pneumonectomy does not differ significantly from normal in O and CO<sub>2</sub> lobar differences Mean difference between lobes in RQ is significantly smaller than in normal persons When he is supine, the mean lobar CO<sub>2</sub> difference in the pneumonectomy patient is significantly smaller than in normal persons, but the mean lobar oxygen difference is not significant Lobar RQ differences for the supine pneumonectomy patient are not significantly different from those in normal persons

Method of Measuring Maximum Breathing Capacities in Individual Lungs by Bronchspirometry is described by J B Clark and G P Maher-Loughnan<sup>7</sup> (London) Of various dynamic methods of measuring ventilation, Kennedy's estimated flow rate at 40 breaths a minute (EFR<sup>40</sup>) is accepted as practical for use in the tuberculous patient for subjective difficulty is rarely experienced by patients in providing the six to eight maximal expiratory efforts required The method advocated is to obtain by bronchspirometry the contribution of individual lungs, subjected as each is to the same limiting factor of cross section of the tube This contribution, expressed as a ratio, can then be applied to the true flow rate measured by spirometry without intubation The method is rapid adding only five minutes to the period of intubation normally needed for other bronchspirometric measures These dynamic measurements of ventilatory power should supplement, not replace other methods of assessing respiratory capacity

TECHNIC—After intubation for bronchspirometry, routine data are obtained on a slow moving drum then for EFR<sup>40</sup>, the fast gear is engaged After careful instruction and trial the patient is asked to give six to eight maximal expirations into the circuit after a pause another six to eight maximal efforts are called for, and exceptionally, if results are not consistent more are recorded The

tube is withdrawn and the patient is encouraged to cough and clear all secretions. After a few minutes of rest he is told to breathe into a closed spirometer circuit and orthodox LFR<sup>16</sup> and vital capacity tracings are obtained at the same session.

Separate lung assessments can be performed with reasonable constancy furthermore less than maximal efforts provide this same constancy of ratio which is important when considering an intubated subject. Differences between additive bronchspirometry totals and figures measured by spirometry reflect two variants cross sectional areas of the bronchspirometry tubes and of the patient's trachea and bronchus.

► [One of the most important considerations in pulmonary resections is the question of whether or not the patient is likely to become a respiratory cripple after the resection. A convenient and reliable test for pulmonary function before the operation is therefore much to be desired.—Ed.]

**Treatment of Ventilatory Insufficiency after Pulmonary Resection with Tracheostomy and Prolonged Artificial Ventilation.** Major surgery can be carried out on tuberculous patients with ventilatory insufficiency (breathing capacity as low as 18 L/minute). Most will have as pronounced ventilatory insufficiency as before operation but the sputum may become negative and they may be able to work. In immediate postoperative management artificial ventilation may be extremely important; this may be intermittent for short periods during the first days until the patient regains sufficient strength to keep the carbon dioxide content down by his own breathing. In some it may be necessary to use artificial ventilation continuously for more than a week or so when there is pneumonia in the only functioning lung. Viking Olov Bjork and Carl Gunnar Engstrom<sup>8</sup> (Stockholm) describe the use of artificial ventilation in connection with antibiotic therapy in two patients with extensive infiltration of the only remaining lung and in one who had compensated ventilatory deficiency before operation and in whom only destroyed nonfunctioning portions of lung were removed. In the first two artificial ventilation was used continuously for six days and in the last intermittently.

Intratracheal aspiration with a nasal catheter is used intermittently in patients with low maximal breathing capacity i.e. 20-35 L/minute. If the patient does not improve and CO<sub>2</sub> retention develops despite frequent aspirations

tracheostomy is performed. This is always advisable if arterial  $\text{CO}_2$  tension is over 70 mm Hg.

The best function test postoperatively is direct measurement of arterial  $\text{Po}_2$  and  $\text{Pco}_2$ . A low  $\text{Po}_2$  with normal  $\text{Pco}_2$  may indicate a secretion retention with atelectasis and shunting of blood through nonventilated alveoli. Then repeated aspiration has to be done, if necessary, through a tracheostomy. If, conversely,  $\text{Pco}_2$  is very high, it is due to ventilatory insufficiency, and tracheostomy is immediately required. If  $\text{Pco}_2$  still remains high, artificial ventilation has to be added as the last recourse. The tracheostomy cannula is provided with a rubber cuff to make an airtight connection with the respirator, which is used intermittently or continuously, as findings indicate.

In patients with abnormally functioning lungs, careful control in arterial blood of carbon dioxide tension, pH and carbon dioxide content (plasma) is necessary, both to acquire proper indications for tracheostomy and artificial ventilation and for adjustment of the latter. As the patient gradually gets stronger, he can, for increasing periods, take over the work of respiration.

► [Seems like a good idea—Ed.]

**Architectural Reconstruction of Lung after Partial Resection of Pulmonary Parenchyma** is described by E. Forster, E. Roegel, M. Assouad and E. Wolf<sup>9</sup> (Strasbourg, France). Complete re-expansion of the residual pulmonary parenchyma after partial resection of the lung is essential for quick cicatrization, good functional recovery and healing without empyema or bronchopleural fistula. Re-expansion depends on mechanical and anatomic factors. An essential mechanical factor is the maintenance of patent bronchi, which permits air to reach the terminal bronchioles to ensure ventilation of the alveoli. The quality of the pulmonary parenchyma is an anatomic factor that facilitates or hinders re-expansion. Factors that play a role in refilling of dead space after partial resection are (1) hyperexpansion of residual parenchyma, possibly because of elasticity of the tissues; (2) elevation of the diaphragm, which, depending on its integrity, diminishes the volume of the hemithorax; and (3) displacement of the mediastinum, of which the

<sup>(9)</sup> J. Thorac. Surg. 31:217-225, February, 1956.

mobility and ability to shift contribute also to refilling of the residual space.

It is easier to obliterate a dead space by shift of a mobile organ, diaphragm or mediastinum than by hyperexpansion of the parenchyma, except when the pulmonary tissue is healthy and elastic, which is rare in adults. A pyramid-shaped space of removed lung is hard to refill. Refilling of the hemithorax is not difficult if after the operation the remaining lung is in contact with rigid elements of the thoracic cavity and distant from mobile structures.

**TECHNIC.**—The lung is completely freed from its parietal fixation, and if necessary its decortication, to ensure a re-expansion that will be well equilibrated and will involve all segments, thus decreasing tension on the areas adjoining the operative zone. The opening or completion of interlobar fissures also results in equal distribution of tension each lobe has to support. It allows the bronchial tree to open and distributes to each of its elements the corrective role of refilling the dead space. Rotation of a segment or a lobe around its bronchial axis brings it in the required new position. Fixation of the rotated lobe or segment is done with a series of stitches fixing the raw intersegmental or interlobar surfaces together. The endothoracic procedure is concluded by securing the lung to the chest wall with a few stitches if necessary. All manipulations are done with the lung well inflated.

The procedure has been used in lobectomies and segmental resections in 136 patients, with good results. Post-operative bronchograms did not show bronchial kinking but only wide incurvations.

**Bilateral Bronchography: New Material and Technic.** Cesare Gianturco and George A. Miller<sup>1</sup> (Urbana, Ill.) advocate the use of dionosil oily, a 50% suspension of the crystals of n-propyl ester of 3:5-diiodo-4-pyridone-N-acetic acid in arachis oil, for bilateral bronchography using a new technic. Dionosil oily is no more irritating than iodized oil and requires no more anesthetic. Since it does not penetrate the terminal bronchioles or the alveoli and is expelled after hydrolyzation without liberation of free iodine, it can be used in iodine-sensitized patients.

A rapid injection technic, under local anesthesia, using an intratracheal catheter inserted through a curved instrument is recommended. The catheter is positioned about 2 cm. above the carina and is checked fluoroscopically with the patient supine. Bilateral bronchography is performed by

(1) Radiology 65 57-60, July, 1955

injecting 8-20 cc on each side in four to six seconds, with the patient in lateral decubitus, and tilted about 10 degrees. The purpose of rapid injection is to fill the dependent main bronchus and cover the mouths of all its branches at once so that the opaque material is aspirated toward the periphery and attains a uniform distribution throughout the bronchial tree. Rapid injection must not be made if the catheter tip is lodged in one of the minor bronchi. A few seconds after one side is filled, the patient is turned on the opposite side for injection of the other main bronchus. After a rapid fluoroscopic check, additional material may be injected in localized areas, if needed.

As soon as the injection is finished, films are taken with the patient upright in posteroanterior and slight right and left oblique positions, with Camp grid cassettes for better contrast. The films show the larger bronchi in double contrast, and distribution of the opaque material in the lesser branches is usually uniform.

With this technic, 25 bilateral bronchograms were obtained. Patients experience no drowning sensation or other great discomfort because air is still present in the peripheral branches when the contrast medium fills the larger bronchi. As air is absorbed by the lung, the medium is aspirated toward the periphery but, before reaching it, is spent almost entirely in wetting the bronchial walls. Very little material reaches the smaller ramifications if the amount injected has been correctly estimated, and there is little or no interference with function of the lungs.

**Is Bronchiectasis a Surgical Disease? Late Results of 145 Operations, Clinical and Bronchographic Study.** J. Mathey, J. J. Galey, G. Oustrieres and G. Vermeil<sup>2</sup> reviewed results in 145 patients with bronchiectasis operated on between 1946 and 1953 to determine the present day mortality rate for pulmonary resection in this condition, proportion of favorable results, relation of various factors to the result and what conclusions should be drawn regarding operative indications and postoperative prognosis.

Four patients (27%) died as a result of accidents directly related to operation—hemorrhage caused by injury to the inferior pulmonary vein, postoperative anoxia, postoperative

hemorrhage of undetermined cause and biopleural fistula. Two of the deaths occurred in the first 10 patients operated on. If these 10 operations are excluded, operative mortality is 1.4%, in the last two years, 1952-53, there were no operative deaths. Secondary mortality, i.e., deaths not related to bronchiectasis, those due to pulmonary tuberculosis and those due to complications of residual bronchiectasis, can be virtually eliminated by treating the patients systematically with antituberculous drugs after operation, by not performing palliative operations on patients with diffuse forms of the disease and by reoperating whenever possible on patients with residual bronchiectasis or recurrent disease.

In addition to the patients who died, four were lost to follow-up, leaving 133 in whom evaluation of late results was possible. Of these patients, 38 of whom have had one or more postoperative bronchographic examinations, 91 are cured, 24 are greatly improved and only 18 had therapeutic failure. Since the 24 who are improved are able to work regularly and have no incapacitating cough, they may be added to the 91 cured patients, making the percentage of success 86.4%. When only patients with unilateral disease are considered, results are still more favorable, with 90.6% success and 72.9% complete cures.

The most important causes of failure or only partial success seem to be errors in the taking or interpretation of preoperative bronchograms and various postoperative complications, especially atelectasis and associated lesions of the upper respiratory tract. Prognosis for patients with bilateral bronchiectasis differs greatly, depending on whether the lesions are unevenly distributed or are substantially the same on both sides. The authors believe that when both sides are equally affected, both should be operated on, but when the lesions are predominantly on one side, operation on that side alone will almost always result in success. Although surgery cannot be used on all patients with bronchiectasis, it is the only radical cure for the condition and since the risk is slight and results are favorable in more than 85% of the patients, it should not be rejected in any but incurable cases.

► [To any surgeon who went through the terrible experience of the bronchiectasis of the 1920's that followed the pandemic of streptococcal pneumonia of 1917-18, these results seem almost incredible. Again there

is no mention of a complicating infection of the nasal sinuses. There seems to be no doubt that the bronchiectasis seen today is much less severe than that of the epoch following World War I—Ed.]

**Indications for Surgery in Bronchiectasis**, discussed by J. T. Chesterton<sup>3</sup> (Sheffield), include (1) gross bronchiectasis, (2) bronchiectasis associated with a definitely collapsed airless lobe or segment and (3) bronchiectasis associated with definite symptoms, i.e., cough, sputum, recurring episodes of infection, recurrent hemoptyses and general debility, which in the adult interfere with work and leisure, in the teen-ager are progressive and in the child show no improvement during summer months. These primary indications require qualification by type of bronchiectasis, its extent, age of patient and clinical course.

Cylindric bronchiectasis is sometimes reversible. Hence, unless indications are clearcut, this type should be treated conservatively for at least six months. In nearly 60% of cases, bronchiectasis is not associated with marked collapse and operative results are comparable to those with complete collapse. Unilateral disease presents no difficulty. The principle in treatment of bilateral disease is that the area of two normal major lobes (upper or lower) should be conserved. Surgery can occasionally give relief in diffuse bronchiectasis, provided one severely collapsed lobe is the main source of retained secretion and hemorrhage. Usually all bronchiectatic areas should be removed, but whittling out every bit of dilated bronchus, merely because it is dilated, is of doubtful value.

The younger the patient when operated on, the more likely is recovery of normal surface area and pulmonary blood flow. Indications against early operation, however, are increased risk of postoperative tracheobronchitis, related to length of anesthesia and frequent recurrence, related to allergic background and congenital weakness of the lungs. Surgery is preferable after age 9 or 10, unless compelling indications necessitate resection earlier, when the added risks must be accepted.

Clinical features suggestive of increased risk of postoperative morbidity and recurrence of bronchiectasis are (1) recurring episodes of "pneumonitis" in nonbronchiectatic areas (breakdown in protective mechanism), (2) deficient movement after adequate physiotherapy, of nonbronchi-

(3) Brit. J. Tuberc. 49:174-178, July 1955.



ectatic areas (fibrosis), (3) persistence of patchy areas of iodized oil for some months in nonbronchiectatic areas (deficient drainage), (4) obviously inadequate bronchial drainage after prolonged courses of antibiotics (resistance of organisms and hypersensitivity of patient), (5) long stay in medical wards, where doubt is engendered in patients, who become more nervous and less co-operative and (6) presence of acute infections and obstructions in other parts of the respiratory tract. Ordinary nose and throat sepsis usually diminishes and is more susceptible to treatment after resection of the lung for bronchiectasis.

Apparently either tracheobronchitis or bronchiectasis may be the cause of the other, but often they have no relation except an allergic basis or a congenital or acquired inclination to bronchial infection. Naturally this diathesis is not affected by resection, surgery only removes the bronchial cesspool. In well selected cases, this improves the patient's condition but it cannot cure the cough. When tracheobronchitis is consequent on bronchiectasis, bronchial infection is usually most marked in the vicinity of bronchiectasis and tends to clear more readily with repeated aspiration and appropriate antibiotics. Nevertheless, about half the cases with marked tracheobronchitis presumed due to bronchiectasis later recur either in episodes or permanently. Hence justification for surgery is great lessening of expectoration and freedom from hemoptysis.

► [It is gratifying that Chesterman recognizes the importance of tracheobronchitis in the symptomatology of bronchiectasis. His statement that about one half of the cases with that feature prominently present tend to recur is more in line with older experience than are most of the present day writings on the subject of bronchiectasis. If there were an effective treatment for nasal sinus disease much of the difficulty encountered with tracheobronchitis would disappear.—Ed.]

**Prognosis of Bronchiectasis after Surgical Resection,** based on analysis of results in 255 cases (221 with satisfactory follow up) is discussed by Robert L. Ginsberg, Jack C. Cooley, Arthur M. Olsen, John W. Kirklin and O. Theron Clagett<sup>4</sup> (Mayo Clinic). Most patients were under 30, but only 5% were operated on before age 10. Since it has been reported that very few patients live beyond age 40 it is interesting that about 10% in this series were 40 or older. Of 221 patients 40% were male. Cough was the pre-

senting symptom in all but five patients, 57% had hemoptysis varying from intermittent rusty sputum to repeated frank hemorrhages. Bronchiectasis was bilateral in 34%, right-sided in 24% and left-sided in 42%. In eight, there was nonobstructive bronchiectasis of the right middle lobe.

After unilateral resection in 213 patients, results were good in 76%, fair in 15%, poor in 5% and death occurred in 4%. Following bilateral resection in eight, results were good in 37%, fair in 50%, poor in 13% and no deaths occurred. Of nine deaths, three occurred three months to two years after operation, from progressive sepsis. Of six hospital deaths, four were due to cardiovascular failure, one to hemorrhage and one to sepsis that occurred six days postoperatively.

A good result was obtained in 82% of patients in whom there was no known residual disease, but in only 68% of those in whom there was ipsilateral disease. Contralateral residual disease does not seem to alter the prognosis greatly, of 57 patients with such disease, 81% obtained a good result. Results of bilateral resection were disappointing, despite selection of patients expected to have a favorable outcome. Pneumonectomy, in general, was followed by excellent results. Of 18 patients, 14 had good results, 1 a poor result and 3 died. One death on day of operation occurred in a patient for whom the surgical risk was known to be great because of severe sepsis and hemoptysis. The other two deaths occurred late, following progressive pulmonary sepsis and insufficiency.

Of 57 patients who required postoperative bronchoscopy because of retained secretions, 61% had a good result, compared with 80% of 164 patients who did not have retained secretions. Of patients with residual disease and retention of secretions, results were good in 60%, compared with 83% with residual disease and no retention. In those with ipsilateral disease, only 25% of patients with retained secretions responded well, whereas 95% of those with no retention had a good outcome. In the group with no residual disease 65% with retention and 88% with no retention were improved.

Of 46 patients with only fair or poor results, about half had one or more significant postoperative complications,

most often retention of secretions. In about one third of this group bronchograms were technically inadequate or interpreted incorrectly. Residual bronchiectasis was found in over half the patients with unsatisfactory results; new bronchiectasis was seen in about a third. If cases of new and progressive disease are combined, about an eighth of the patients had extension of bronchiectasis, this is in conflict with usual opinions. Postoperative complications do not preclude an excellent result, but they seem to reduce the chances for it; hence they have a critical bearing on prognosis.

► [It seems amazing that a report like this would be published without a word of comment about the nasal sinuses. If those sinuses are badly diseased the patient will certainly have a chronic bronchitis with cough and purulent sputum even if there is no demonstrable bronchiectasis. The prognosis is greatly influenced by the condition of the sinuses. This has been known for many years and some good work was done on the relationship of sinus disease to bronchiectasis 30 years ago at the Mayo Clinic by Lemon and others—Ed.]

**Endoscopic Treatment of Bronchial Fistulas** after pulmonary resection in 10 patients is reported by Dezso Kaszay, Daniel Dimitrov Szokodi and Georg Mihok<sup>5</sup> (Univ. of Budapest). The patients were classified into three groups: the first consisting of three in whom a small ulcer had developed from an infected suture. Bronchoscopic removal of the suture followed by one or two cauterizations of the bronchial stump with trichloroacetic acid resulted in closure of the fistula within 8-10 days. The second group consisted of four patients with profusely ulcerating centrally situated nut-sized abscesses often resulting from contraction of a central hilar empyema. These lesions are difficult or impossible to drain through an external approach. Healing of the fistula requires evacuation of the abscess with consecutive shrinking of the cavity. Treatment of this group is the most difficult.

Man 24 showed opening of the bronchial stump six days after right lower lobectomy. X-ray revealed a nut-sized abscess cavity near the hilus with fluid. Attempted thoracic puncture was unsuccessful. At bronchoscopy a massive abscess of the middle bronchus was drained and a ureteral catheter inserted into the fistula leading to the stump of the lower lobe bronchus yielded about 10 cc pus. The cavity was irrigated with saline containing 40,000 units of penicillin and 100 I.C.M. streptomycin and this procedure was repeated two days later with removal of a similar quantity of pus. Four days later

purulent discharge had decreased and after another four days, practically disappeared. The fistula then was cauterized with trichloroacetic acid. Fistula and cavity disappeared after three cauterizations.

In the third group (three patients), the bronchial stump communicated with an empyema cavity reaching to the thoracic wall. Drainage was accomplished by thoracic puncture, and the fistula was healed by antibiotics and endoscopic cauterization. One of these patients died of metastatic carcinoma six days after drainage and cauterization, and autopsy showed complete healing of the bronchial stump and closure of the fistula.

Primary consideration in treatment of these fistulas is drainage of purulent secretion. Cauterization of the opening is of secondary importance.

► [Nobody could disagree with the final conclusion—Ed.]

**Middle Lobe Syndrome** is described by Gustaf E. Lindskog and Harold C. Spear<sup>6</sup> (Yale Univ.). Atelectasis with chronic pneumonitis involving the right middle lobe due to compression of the middle lobe bronchus by enlarged lymph nodes was named "middle lobe syndrome" by Graham, Burford and Mayer who first recognized the syndrome. Compression bronchostenosis with atelectasis and pneumonitis may occur in any lobe. The right middle lobe is singularly susceptible because its relatively small lobar bronchus is surrounded by a cluster of lymph nodes that drain, not only the middle lobe proper, but also lymphatic tributaries from the adjacent lower lobe, and because the lymph nodes may enlarge with an inflammatory process within either the middle or the lower lobe. The small caliber of the middle lobe bronchus and its emergence at almost a right angle from the intermediate bronchus hamper adequate drainage. In most patients there is no bronchial compression and the bronchial obstruction results from edema and inflammation of the bronchial wall proper. Bronchiectasis is frequently secondary to long standing bronchial obstruction with distal infection.

Middle lobe syndrome occurs in an equal sex ratio and at any age. The main symptoms are chronic cough, recurrent respiratory infections, wheezing, hemoptysis, chest

are no symptoms, and x-ray findings are the only indication of the condition.

The x-ray findings consist of a triangular or quadrilateral shadow, often well visualized only on right lateral films in the right lower anterior lung field. The horizontal fissure is depressed. frequently, hilar lymphadenopathy with or without calcifications is found. The findings should be differentiated from interlobar effusion and from a prominent right border of the heart with elevation of the right leaf of the diaphragm. Lipiodol® bronchography may help to confirm



Fig. 2.—Anterior and lateral views showing hilar lymphadenopathy on the right with calcification, together with atelectasis of middle lobe and residual tuberculous infiltration of lower lobe (Courtesy of Lantskog, G. E., and Spear, H. C. *New England J. Med.* 253:489-495, Sept. 22, 1955.)

obstruction or atelectatic clumping of the lobar or segmental bronchi, and possibly to demonstrate secondary bronchiectasis. Bronchoscopy often reveals inflammatory stenosis of the middle lobe bronchus, but may be indeterminate.

Definitive diagnosis of middle lobe syndrome can be made only by surgery and after examination of the resected specimen and not on the basis of clinical, bronchoscopic and radiologic findings. A study of seven cases with some clinical and radiologic features in common with middle lobe syndrome revealed a different pathologic entity in each. The lesions included nonspecific atelectasis and chronic pneumonitis with secondary bronchiectasis, bronchogenic carcinoma, atelectasis and organizing pneumonitis second-

ary to tuberculous hilar lymphadenitis, parenchymal tuberculosis, chronic abscess, with organizing pneumonitis, acute pneumonitis, with resolution, and lipoid pneumonia. Except for resolving pneumonia each of these lesions has its own sequelae, which may be progressive and sometimes even fatal.

Boy 7, had been treated in a sanatorium for four years for primary pulmonary tuberculosis of the right lower lobe with associated hilar lymphadenopathy. He had a chronic cough. X-ray films showed extensive right sided hilar lymphadenopathy, with calcification, and atelectasis of the middle lobe and residual tuberculous infiltration in the right lower lobe (Fig 25). Cultures were negative. Bronchoscopy revealed the middle lobe orifice to be occluded with granulation tissue. Bronchial secretions were negative for acid fast bacilli by smear. Streptomycin and para-aminosalicylic acid therapy produced slight clearing of the middle lobe atelectasis. Bronchoscopy following this therapy showed a definite cicatricial stenosis of the middle lobe orifice. Bronchograms revealed bronchostenosis. The right middle lobe was resected. Pathologic study revealed slight dilatation of the segmental bronchi and extensive parenchymal consolidation with focal organizing pneumonitis. There was no histologic evidence of tuberculosis and multiple acid fast stains were negative. He recovered.

**Middle Lobe Syndrome** Fernando Paulino<sup>7</sup> reports three surgical cases. No extrinsic hypertrophic lymph nodes were found, but intrinsic stenosis produced by thickening of the bronchial wall (stenosing endobronchitis) was present. In two patients the lesions were tuberculous. Careful dissection of the peribronchial lymph nodes showed no induration or adhesion to the diseased bronchus, which contradicts Graham and Brock's hypothesis that stenosis in the middle lobe syndrome results from external compression. Another patient without previous pulmonary symptoms had typical atelectasis of the middle lobe following influenza. X-ray examination 20 days later showed complete regression of atelectasis.

Incidence of the syndrome has increased considerably in recent years and it accounted for 18% of lobectomies performed by Paulson. It affects both sexes and both adults and children. Pathologically there is bronchial stenosis (extrinsic or intrinsic) and pneumonitis of the middle lobe with atelectasis, fibrosis and at times bronchiectasis. Hypertrophic sometimes calcified lymph nodes may surround and compress the middle lobe bronchus. The bronchial wall may be thickened so that the lumen is completely ob-

(7) Rev bras I cir 30 111 113 1955

structed Tuberculous lesions in lymph nodes, bronchi and parenchyma have been found in about 50% of reported cases. An identical syndrome affecting the lingula on the left side corresponds to the middle lobe syndrome on the right. Anatomic factors favoring development of the syndrome are extent and relatively small caliber of the bronchus in relation to other lobar bronchi, lymph nodes surrounding this short small bronchus and the position of the bronchus of the middle lobe which does not facilitate drainage by gravity.

Most frequent symptoms are cough, fever, chest pain, expectoration and hemoptysis. Generally, cough is worse in the dorsal decubitus and better in the ventral or vertical position. Wheezing and dyspnea are infrequent. Physical findings are those of chronic pneumonitis, with acute exacerbations. Thoracic teloradiography shows reduced transparency in the inferior half of the hemithorax. Lateral roentgenogram is indispensable and usually is diagnostic. Atelectasis of the middle lobe is usually evident as a dense triangular shadow situated in the anterior portion of the hemithorax. Bronchoscopy should always be done to exclude obstructive carcinoma. Such malignant localization is rare, but the author observed one case, confirmed histopathologically. Bronchoscopy in the author's cases revealed mucosal edema and bronchial stenosis. Bronchography is unnecessary if diagnosis can be established by lateral roentgenograms and bronchoscopy. When performed, it reveals a "stop" in the middle lobe bronchus or stenosis with bronchiectasis. Search for tubercle bacilli, neoplastic cells and identification of organisms in the sputum and aspirated secretion should be carried out routinely, as in all patients with pulmonary symptoms.

In acute cases, treatment should consist of antibiotics, antiallergic agents, rest and nebulizers. In chronic cases and those resistant to medical treatment, lobectomy should be done.

► [The author does us a slight injustice in ascribing to us the thought that in all cases of this syndrome the bronchial stenosis is due to external compression from enlarged lymph nodes. Indeed in our original article (Graham E. A., *et al.* Postgrad Med 4:29-34 July 1948) we state: 'The impression is not to be left that the stenosis results purely from the pressure of lymph nodes. The bronchial stenosis may not be due entirely to pressure by enlarged glands but may in part be caused by spread

of infection through the bronchial wall from the glands with resultant edema and even, at times, stricture"—Ed]

**Results of Pulmonary Resection for Tuberculoma** M Bernard, P Galy and E C Saubier<sup>8</sup> (Lyons) present an analysis of 82 operations performed during the period 1948-54. Four patients were under 20 years, 47 between 20 and 30, 23 were 30-40 and 8 were over 40. There were 53 females. Lesions were located in the upper lobe in 62 and in the lower in 20 (four in Fowler's lobe). Most were solid tuberculomas, only 12 had excavated lesions. Three of these had segmental resections, three inferior and six superior lobectomies. Only 13 patients had bilateral lesions, 5 had additional lesions on the same side. Most patients had had previous treatment with streptomycin, para aminosalicylic acid and isoniazid. In all cases, antibiotics were administered for at least two weeks before and after operation. Superior lobectomy was done in 35, inferior lobectomy in 16 and segmental resections in 31, of which four were wedge resections for limited superficial lesions.

On the whole, operative conditions are more favorable than in other types of tuberculosis for which resections are performed. Nevertheless, difficulties may be encountered especially changes involving the hilus, which render dissection difficult and dangerous. In 18 cases there was gross adenopathy, inflammatory or sclerous and sometimes calcified, which made operation difficult. In one case there was a gangliobronchial fistula. In five, there was severe inflammation of bronchi, with stenosis in one.

There was no surgical mortality. The only significant complications were an infection in the wall, rapidly controlled by antibiotics, and two incidences of empyema, one occurring two months and the other three years after operation which were easily cured. There were also two incomplete re-expansions that required partial thoracoplasty, one after lobectomy and one following segmental resection. Late results were excellent in these two cases.

Late results were satisfactory. Three patients had full term pregnancies without complication. Most patients returned to work three to six months after operation. Only two patients had recurrence within a year after superior lobectomy and after segmental resection. One was a man,

(8) Presse med. 63 893 894 June 11 1955



29, who was treated at least six months before operation. The other patient, a woman, 33, had an earlier operation. Both had excavated lesions. They were given medical treatment and a second operation was planned for the man.

The authors emphasize that every round, filled tuberculous x-ray shadow is not tuberculoma in the strict sense. Various changes may display the same appearance. Tuberculoma is defined as a caseous, altered, stratified focus of definite size, this excludes coalescent foci and filled cavities, which differ from tuberculoma in origin, spontaneous progression and postoperative prognosis.

**Decortication of Lung in Tuberculous Disease: Study in 43 Cases.** T. Savage and H. A. Fleming<sup>9</sup> (Glamorgan, Wales) state that *constrictive pleuritis may follow primary tuberculosis or artificial pneumothorax, and causes loss of respiratory function, empyema and displaced mediastinum. Decortication of the lung is excellent treatment, but failure of the lung to re-expand is usually due to inability to deal with air leaks and fluid collecting in the pleural space in the early postoperative period. The end results should be good if postoperative treatment is carefully carried out.*

Indications for decortication are tuberculous empyema with no detectable disease in the underlying lung, disease treatable by chemotherapy, partial resection or thoracoplasty, or thickened pleura, giving rise to appreciable loss of respiratory function. Contraindications are stenosis of a main bronchus, though decortication plus lobectomy in lobar bronchostenosis is possible, severe uncontrolled disease in the underlying lung, or severe contralateral disease.

Decortication was done in 43 patients (10 women), aged 8-53 who had had the disease for 3 months to 20 years. Indications were primary tuberculous pleurisy and effusion in 20, pleurisy and effusion complicating artificial pneumothorax in 22 and spontaneous rupture of cavity in a free pleura in 1. The pleural fluid was positive for *Mycobacterium tuberculosis* in 26.

Preoperative preparation includes costal and diaphragmatic breathing exercises, a plaster cast that hyperextends the affected side and streptomycin, para-aminosalicylic acid

(9) Thorax 10 293 308 December 1955

and isoniazid for three months. None of the patients had positive sputum test results at the time of surgery.

At surgery, all of the thickened pleura that can be removed is stripped from the lung and parietal wall of the chest. The lung is expanded as much as possible. In some patients, further surgery was necessary, thoracoplasty was done on four, segmental resection on eight and wedge resection on one. Blood is administered during surgery as necessary. The chest is drained with a basal tube and a long tube inserted in the midaxillary line in either the 9th or 10th intercostal space and held against the inside of the chest wall by a catgut sling. The tubes are of firm rubber, with internal diameter of  $\frac{1}{4}$  in and a wall  $\frac{1}{10}$  in thick, to prevent collapse when strong suction is used postoperatively. All patients received antibiotics for six months postoperatively.

The lung should be fully expanded postoperatively and kept so until all air leaks have ceased. Strong continuous suction is applied through water-sealed bottles to all drainage tubes. The degree of suction is about one atmosphere (30 in Hg). The tubes are not removed until they have ceased functioning. On the second or third postoperative day, the patient is put in a special hyperextension plaster. This tends to make the mediastinum fall to the opposite side, the diaphragm is carried caudally and the ribs are stretched apart. The patient is kept in the plaster cast, except for meals, for three to six weeks and this is used for sleeping for three to six months. Breathing exercises are used.

There were no deaths, and the morbidity was low. Complications included nontuberculous drainage tube tract infection in three, nontuberculous bronchopleural fistula and empyema in one, persistent pleural space for three to four weeks in six, phrenic nerve accidentally injured in three, reactivation of disease in two and hemothorax in one.

The patients were followed for 6 months to  $4\frac{1}{2}$  years. Obliteration of the pleural space occurred in all 34 with empyema or uninfected persistent pleural space. In no case was there greater mediastinal shift postoperatively than there had been preoperatively. Disability due to displaced mediastinum was seen in only one patient. All of 24 patients

with shortness of breath on mild to moderate exertion pre-operatively were improved. Improvement in diaphragmatic movement occurred in all patients except those with phrenic nerve injury. Radiologic improvement of varying degree was seen in all. The maximum breathing capacity improved in all but 2 of 25 patients. Differential lung function tests in 18 patients showed improvement in all but 4.

It is concluded that in selected cases of tuberculous pleural disease, decortication of the lung is a safe and satisfactory procedure, removing infection, obliterating space, re-expanding the lung and improving function.

**Treatment of Tuberculous Empyema.** D. Ruiter<sup>1</sup> (Ap-pelscha, The Netherlands) states that tuberculous empyema may follow spread of disease from the lungs, pleura or ribs or may follow surgery, such as pneumothorax, pneumolysis, speleotomy, cavity suction drainage, extrapleural pneumo-thorax, thoracoplasty and resections of lungs or parts of lungs. A bronchopleural fistula, often the main factor in causing tuberculous empyema, was found in 35% of 77 patients (excluding empyema following resection) and in 4.25% of 400 patients following resection. Of the latter, 12 also had empyema. The prognosis of bronchopleural fistula without a specific infection of the pleura is good provided it is treated in time and correctly. Treatment should include suction drainage, measures to control nonspecific infection and, if necessary, plastic correction including three to four ribs.

Tuberculous empyema is difficult to treat and tends to relapse. It is important to distinguish two forms, i.e., tuberculous empyema with and without bronchopleural fistula. Pus must be studied bacteriologically. A fistula can be detected by the methylene blue test and by determination of the tension in the empyema cavity, if necessary after aspiration of air and drainage of pus. The marked negative tension resulting from drainage is unlikely to be maintained longer than 30 minutes in the presence of a fistula. If no pulmonary fistula is demonstrable, empyema is treated preferably by the closed method, even when specific infection exists. This consists in puncture, lavage and local drug treatment. Conservative treatment is aimed at controlling

(1) Arch. chir. neerl. 7:89-104, 1955.

inflammation and allowing the lung to expand. If a bronchial fistula is present, a drain should be inserted into the empyema cavity and suction used to prevent aspiration of pus into unaffected parts of the lung. Active treatment, i.e., resection of the part of the lung in which the fistula and pulmonary changes are localized, is deferred during the acute stage until suction drainage and local treatment have decreased the operative risk. If there are permanent lung fistulas, duration of conservative treatment should not exceed two to three months.

Local drug therapy in both open and closed irrigation methods includes neutral solutions, the enzymes streptokinase and streptodornase, streptomycin, para aminosalicylic acid and conteben\*. Combinations of streptomycin, PAS and isoniazid have proved effective.

Surgical treatment is difficult because of the frequently encountered thick rigid walls firmly adherent to adjacent parts. Streptomycin and penicillin are used, with isoniazid or PAS postoperatively. Drainage is continued as long as necessary using suction. Should exudates form, punctures and local drug treatment are used.

Operations for tuberculous empyema combined with bronchopleural fistula include thoracoplasty (which yields good results only when the parietal pleura is still mobile), plastic correction (used in local empyema especially after pulmonary resection), Schede's modification of thoracoplasty (resection of ribs at the level of the empyema and removal of parietal pleura done in one or two stages), pleuropneumonectomy (performed when active pulmonary disease is present), decortication (sometimes combined with partial pulmonary resection) and pleurectomy (performed when the lung under the empyema shows only dormant or no changes).

With conservative treatment 26 of 37 patients recovered. Of 48 patients who underwent 74 operations including 26 thoracoplasties (16 Schede modifications), 21 pleuropneumonectomies, 6 plastic corrections and 6 pleurectomies (combined with lobectomy in 2), 34 recovered and 6 died. The others were operated on too recently for evaluation. Best results were obtained with pleuropneumonectomies and pleurectomies.

**Bilateral Resection Therapy in Pulmonary Tuberculosis**  
J K Kraan<sup>2</sup> (Appelscha, The Netherlands) states that treatment of bilateral pulmonary tuberculosis is difficult when strict bed rest supported by drug treatment has not led to recovery. Bilateral resection is possible when the disease is well demarcated and the operation will not cause too great a loss of functioning lung tissue. If there are no complications, there need not be any serious loss of pulmonary function. Preoperative examination for localization of the disease must be accurate and the whole course of the disease well known so that no unpleasant surprises will arise during operation. The bacilli should still be sensitive to antibiotics, streptomycin in particular. It is important to examine accurately pulmonary function, both before and after the first operation and after the second operation, for an objective evaluation of results.

Bilateral resection was performed on 14 patients whose disease was confined to at most two segments of each lung so that function was not disturbed. Surgery was first carried out on the side on which, in view of extension and localization of the process, there was the least risk of loss of function, in order to minimize the danger should a complication arise in the second operation. All operations were performed under the protection of streptomycin, also administered for two weeks postoperatively. Patients were on bed rest for four months after surgery and were kept in the sanatorium for an additional four months. They also received para-aminosalicylic acid for two months postoperatively.

All patients had extensive function tests before and six months after surgery. Maximal respiratory minute volume, vital capacity, ventilation reserve, residual volume, oxygen uptake and respiration equivalent using bronchspirometry technics were determined for each lung separately. Six patients have been followed long enough for accurate evaluation. These were all young persons who had positive sputum even though their tuberculosis was only slightly active. All except one had segmental resection only. They did well clinically, and tests revealed only slight loss of function. Although it is not possible to say that all six are cured, the most important foci of infection have been removed and,

with prolonged after-treatment, they have a reasonable chance of winning the fight against the disease with their own defensive powers

**Pneumonectomy in Pulmonary Tuberculosis without Thoracoplasty: Clinical Results and Lung Function Studies**  
J J Hirdes and M W Bosch<sup>3</sup> (Bilthoven, The Netherlands) performed 83 pneumonectomies and 23 pleuropneumonectomies without thoracoplasty in 45 men and 61 women. During sanatorium treatment six patients died, and after discharge three patients had a relapse, one of whom died. Indications for surgery were primary tuberculosis in 3, ulcerative tuberculosis in 8, tuberculoma in 1, tuberculous bronchitis in 13, cavities in 49 and destroyed lung and/or empyema in 32. The causes of death were shock, bronchopneumonia, tuberculous empyema with bronchial fistula, dissemination, heart and lung insufficiency and anuria due to amyloidosis of the kidneys. Empyema occurred in five patients, in three from staphylococci and in two from tubercle bacilli. Only the latter two had bronchial fistulas. Tuberculous empyema with bronchial fistulas developed soon after surgery and could not have been prevented by thoracoplasty. It is believed that there was no connection between the cause of death of the seven patients and lack of thoracoplasty, with the possible exception of one, who died from dissemination.

The technic of closing the bronchial stump and the sensitivity of tubercle bacilli to antibiotics are of much greater significance than thoracoplasty. Two continuous sutures, which cross each other in the same manner as laces of a shoe, close off the bronchus. If edema of the mucous membrane develops or if the patient coughs, these threads constrict still more, preventing leakage. Vascularization of the bronchial stump is not interfered with by these sutures, so within a short time the margins of the mucous membrane grow together. The bronchial stump is also covered with pleura and embedded in the mediastinum. The thoracic cavity is not drained after operation. None of the patients was resistant to streptomycin preoperatively. All were treated with streptomycin, para aminosalicylic acid and isonicotinic acid hydrazide orally and intramuscularly, and intrathoracic injections were given daily.

(3) J Thoracic Surg 30 719 740 December 1955

Complete recovery occurred in 91. Only seven patients still had positive sputum culture that was caused mostly by small foci in the remaining lung, resulting from bronchogenic spread. One patient had an unsatisfactory result and one patient was classified as having a bad result. Two patients had bronchogenic spread to the other lung immediately following pneumonectomy, which reabsorbed in a short time under antibiotics. After discharge, three reactivations occurred, each with the formation of cavities and one patient died. The reactivations were not attributed to stretching of the remaining lung.

The function of the remaining lung was studied in 38 patients more than two years after the pneumonectomy. The vital capacity and total capacity increased. Maximum breathing capacity also increased but to a lesser degree. The usable part of the vital capacity remained stationary. The residual volume was considerably greater in older than in younger patients. In both it diminished with passage of time. Results of the lung function changes in older patients are not due to fibrosis or emphysema, but probably due to mechanical disturbances of expiration.

Thoracoplasty or phrenic exeresis as routine treatment after pneumonectomy for pulmonary tuberculosis is not necessary. Reduction of the thoracic cavity by these procedures is undesirable as it disturbs the breathing mechanism and restricts ventilatory function. By omitting thoracoplasty, the mutilating effect and psychic trauma of this operation on the patient are prevented.

**Left-Sided Bronchotracheal Anastomosis** Viking Olov Bjork<sup>4</sup> (Stockholm) reports direct anastomosis of the left lower lobe bronchus and the trachea after excision of the diseased bronchus. Wide mobilization of the aorta after division of the four upper pairs of intercostal arteries, mobilization of the left subclavian artery, esophagus, trachea and central part of right main bronchus makes the surgery feasible. Direct anastomosis is preferable to plastic reconstruction with dermal graft.

Woman 32 had tuberculous infiltration in the left upper lobe with a cavity. Bronchography revealed considerable narrowing of the left main bronchus from the carina down to the left upper lobe bronchus. The lower lobe bronchus was normal.

With the patient prone, ribs two to six on the left side were divided, the lung was freed intrapleurally and the upper lobe resected. The pulmonary artery was freed from the left main bronchus by sharp dissection from its origin in the main pulmonary artery to its

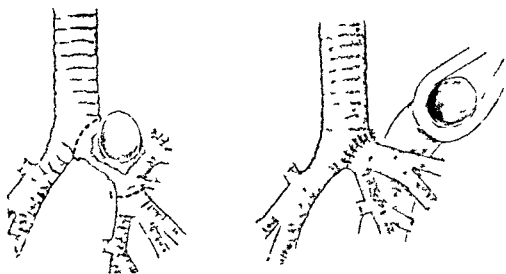
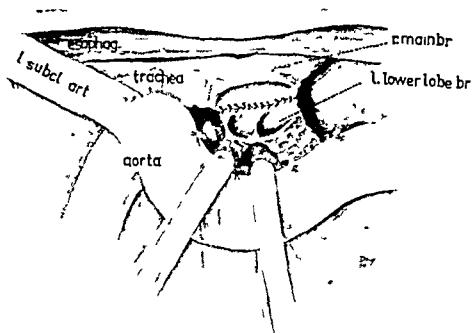


Fig 26—Mobilization of aorta and direct anastomosis between left lower lobe and trachea (Courtesy of Bjork V O J Thoracic Surg 30 492-498 October, 1955)

divisions in the basal segmental arteries. The left main bronchus was dissected as far as possible under the arch of the aorta. The four upper pairs of intercostal arteries were divided and the aorta and left subclavian artery were mobilized forward (Fig 26). The esophagus, the left main bronchus, 5 cm of the trachea and the proximal part of the right main bronchus were dissected free. The left main



bronchus was opened longitudinally in the posterior part. The inferior pulmonary vein was freed but the pulmonary ligament was not divided. The left main bronchus was excised from the trachea and divided just central to the bronchus to the superior segment of the lower lobe. The endotracheal tube was pushed down in the right main bronchus, and an airtight connection to the right lung was obtained. A Potts clamp was applied on the lower lobe bronchus which under considerable traction was approximated to the trachea.

First a row of isolated over and over 00 silk sutures on non-traumatic needles was placed and tied anteriorly. The posterior row of isolated silk sutures was easy to place and tie. The bronchus to the superior segment lower lobe was sutured into the superior corner of the incision in the trachea. The suture line was not covered with a pleural flap. Streptomycin was placed around the suture, and the mediastinal pleura was closed. Bronchoscopy postoperatively showed the anastomosis open for the 9 mm bronchoscope. The patient made an uneventful recovery.

Three months postoperatively, the left lower lobe was well aerated. Bronchography demonstrated a patent bronchotracheal anastomosis and no bronchiectasis. Bronchoscopy was performed four times to remove the silk sutures causing granulomas. After removal of the sutures a well healed anastomosis was seen seven months postoperatively.

**Bronchial Adenoma.** D Kassay, A Bikfalvi and J Baló<sup>5</sup> (Univ of Budapest) report clinical, pathologic and histologic findings in 18 tumors, 14 of which were of solid, or so called carcinoid, type, consisting of solid masses of epithelial cells, with nuclei, form and size of cells generally uniform and relatively scant connective tissue between cells. The stroma contained bundles of connective tissue, usually with hyaline degeneration. One tumor was classified as "glandlike." Another "mixed tumor type" was sharply delimited and covered with a capsule. The generally uniform epithelial cells were arranged in solid masses. There were also cells with appendages embedded in mucus and glands filled with mucous secretion.

In one patient, the tumor extended outside the bronchial wall and within the lumen and contained bone callus, i.e., osteoplastic or chondroplastic adenoma. In another, the tumor tissue removed bronchoscopically showed bronchial adenoma, but thoracotomy revealed numerous disseminated carcinomatous pleural nodules. Of the 18 tumors, 10 were endobronchial benign adenomas, and 3 involving the bronchial wall were of transitional, so called iceberg, type. Localization was peripheral in one and in three could not be

determined. It is concluded that adenomas are not originally malignant but may become so.

The general principle governing therapy is that the adenoma must be removed radically. Choice of operation is influenced by histology, site and extent of tumor, whether it is pedunculated or has a broad base, its relation to surrounding tissues, severity of clinical symptoms and age of patient. For the small projecting or slender-pediced tumor, which is almost always solid, conservative procedures are preferred. Glandular and osteoplastic tumors are considered potentially malignant and require more radical surgery. They usually have a broad base and are located at the apex of the carina, near the bifurcation or in the air tubes. Half the glandular tumors are situated in the region of the carina. Extrabronchial infiltration and extension are rare. Radical surgery must be done if any tumor invades the parenchyma, if metastases (mainly in the regional lymph nodes) are suspected, if histologic findings are inconsistent and if the tumor is difficult to reach endobronchially.

Bronchoscopic treatment is usually merely palliative and is preferable to radical surgery only in a few poor risk cases. When possible, an attempt should be made to remove the entire tumor endoscopically. This assures accurate histologic diagnosis, drainage of the distal bronchial system and ventilation of the lung and prepares for the later surgical attack. Repetition of endoscopic removal is justifiable only in cases unsuitable for surgery.

Therapy consisted of endoscopy alone in two, resection of *bronchus plus anastomosis* in one, *lobectomy* in two, *bilobectomy* in one and *pneumonectomy* in six. The lesion was inoperable in one, and one patient refused surgery. Two patients died before operation could be performed, and the lesions were examined at autopsy.

Histologic diagnosis of first biopsy was correct in eight, and erroneous in six. Carcinoma was mistakenly diagnosed in five, the other false diagnosis being edematous polyp. Local recurrence appeared after endoscopic removal in two patients. The operation was excessively radical in three.

► [According to American standards, the authors apparently are too radical in their treatment. Nowadays we would not perform pneumonectomy in one third of the cases. On the contrary, it is rare to be so radical in the treatment of adenoma. Womack and the editor in 1938 called attention to the fact that these are potentially malignant. At

time we received scant support of the idea. Now, however, the idea is commonly accepted. It is gratifying that the authors of the present article also believe in the potential malignancy of these tumors—Ed.]

**Case of Bronchial Adenoma with Liver Metastasis** is reported by Priscilla Kincaid-Smith and Jean-Jacques Brossy<sup>6</sup> (Postgrad Med School, London)

Woman, at age 58, underwent right middle and lower lobectomy (March 1948) for bronchial adenoma. At a routine follow-up in September 1954, she reported having intermittent diarrhea for 10 weeks, the stools were watery, without blood or mucus. There had been some flatulence but no dyspepsia, pain or weight loss. A tumor was palpated under the left costal margin near the midline. Radiography confirmed the absence of gross disease in the chest. X rays of the digestive tract showed that the stomach and colon were displaced by, but not attached to, the mass. A pyelogram revealed downward displacement of the left kidney, but the calyceal pattern was normal.

The presumptive preoperative diagnosis was pancreatic cyst, but laparotomy revealed a cystic mass, 10 cm in diameter, in the lower edge of the left lobe of the liver. It was easily excised with a thin rim of liver tissue. There were no other tumors in the liver, and the stomach, transverse colon and gallbladder appeared normal. laxness of the hepatogastric omentum and unusual mobility of the tumor had enabled it to project behind the stomach and give the radiologic appearance of a retroperitoneal mass. The patient was well when last seen in March 1955, at age 65.

The microscopic appearance of the tumor was similar to that of the primary bronchial adenoma removed six years previously. Tumor cells were of the same uniform polyhedral type. The only significant difference was the relative frequency of mitoses (approximately 1/high power field). The dense collagenous capsule which surrounded the tumor was invaded at several points. A few infiltrating tumor cells were present in adjacent liver tissue outside the capsule. The pathologic diagnosis was metastatic carcinoid bronchial adenoma.

Increased mitosis in the metastatic tumor, as compared with the primary bronchial lesion, is of interest in view of reports of progression of bronchial adenomas to frank carcinomas and of cases in which diagnosis lay between an adenoma and a carcinoma. Possibly malignant transition may account in part for the rarity of autopsy accounts of bronchial adenoma in the days before bronchoscopy became a routine method of clinical investigation.

**Metastatic Malignant Lesions of Lungs Treated by Pulmonary Resection: Report of 43 Cases** is presented by Rob-

ert I Hood, Jr, Robert P McBurney and O Theron Clagett<sup>7</sup> (Mayo Clinic and Found.) Sex incidence was almost equal (23 males), in contrast to preponderance of males having pulmonary resection for bronchogenic carcinoma. The first pulmonary resection for metastatic malignant lesions was performed in 1941, and other patients in the study were operated on before 1952. Ages ranged from 6 to 67, 58% were in the fifth and sixth decades. Follow-up of 42 patients showed that 18 were living over three years and 11 over five years after operation. Pulmonary symptoms were not significant in 24 patients before removal of their metastatic tumors. Cough was present in 14, this was productive of sputum in 10, and 8 noted hemoptysis. Three complained of pain, two of dyspnea and one of wheeze. In 12 patients whose primary lesions had been removed 3-15 years previously, concern about pulmonary symptoms was the stimulus for seeking medical consultation.

All patients presented x-ray evidence of a nonobstructive pulmonary mass lesion. Except in two, no detectable pulmonary lesion was present at the time of operation for primary tumor. Examination of sputum of 11 patients for malignant cells showed atypical cells in 1 and unequivocal malignant cells in 2, 8 had negative specimens. Preoperative bronchoscopy in 11 patients demonstrated malignant tissue in 5, tissue from another mass showed only inflammation. Bronchoscopy showed narrowing of the right lower lobe in one and bleeding in another. Primary tumors were classed as carcinomas (including teratoma of testis, mixed tumor and hemangioma) in 32 and as sarcomas in 11. The commonest tumor was adenocarcinoma of the bowel—one in the jejunum, four in the colon and four in the rectum. Other carcinomas included teratoma of the testis, four cases hypernephroma and melanoma, three each, adenocarcinoma of the ovary, adenocarcinoma of the breast and squamous cell epithelioma of the cervix, two each, and adenocarcinoma of the uterus, cylindroma of the salivary gland and of the nasal fossa, mixed tumor of the jaw, squamous cell epithelioma of the skin, squamous cell epithelioma of the larynx and hemangioma, one each. There were six cases of fibrosarcoma, three of osteogenic sarcoma and one each of giant cell tumor and Ewing's tumor. /

In two instances, pulmonary metastasis was removed before a primary growth was excised. The interval between the two operations in others varied from 2 to 270 months. In 25 of the 43 cases, pulmonary resection was performed one to five years after removal of the primary growth. Lobectomy was used in 26, pneumonectomy in 12, local excision in 4 and segmental resection in 2. The trend has been toward more conservative surgery. The only hospital death occurred one month after pulmonary resection. Among 41 patients successfully followed, the longest survival was over six years (3 patients), 30 survived over one year, 20 for three years.

Presence or absence of preoperative pulmonary symptoms had little, if any, prognostic bearing. In general, larger lesions were associated with shorter survival. The outlook for patients with carcinoma was somewhat more favorable than for those with sarcoma. Variation in survival among patients with pathologically similar tumors was great. The greater the interval between removal of primary and metastatic tumors, the better the survival. Of 17 patients whose metastatic tumors were removed three years or less after primary operation, 9 (52.9%) survived one year or more. Of 24 patients with over three years between operations, 21 (87.5%) lived one year or more.

Criteria for judging advisability of operation remain obscure. Occasional "cure" is obtained even with highly lethal tumors, i.e. a patient with metastasis secondary to teratoma of the testis was alive without recurrence 39 months after its removal. Extent of the pulmonary resection did not appear to be a factor in length of survival. Conservative resections may have more applicability for metastatic tumors than for bronchogenic carcinoma, since the former are less likely to spread by lymphatic channels. Choice of the less disabling procedure finds further support in the fact that the value of pulmonary resection for metastatic disease remains unestablished. The palliation offered is noteworthy, and prolongation of life is often gratifying.

**Exfoliative Cytology and Pulmonary Cancer.** Histopathologic and Cytologic Correlation was made in 501 patients admitted to Barnes Hospital, 1948-53, by Harlan J. Spjut, Dorothy J. Fier and Lauren V. Ackerman<sup>8</sup> (Washington

Univ.) For tissue confirmation there were 318 bronchial biopsies, 95 other biopsies, 163 pneumonectomies, 35 lobectomies, 126 exploratory thoracotomies and 35 autopsies. Cytologic smears studied numbered 1,269, including 905 sputa and 364 bronchial washings. Of the former, 27.1% and of the latter, 31.6% were positive. On a case basis, over-all percentage of positive reports was 57.8% and with an optimal number (three or more) specimens, 76.6%.

Of 318 bronchial biopsies, 211 (66.3%) were positive. Only 28% of positive biopsies were in operable cases. Lower lobes yielded the highest percentage of positive smears (bronchial washings). The highest percentage of positive sputa was obtained from the left upper lobe.

Cytologic examinations are of value in diagnosis of peripheral pulmonary cancers. Lesions 2-3 cm in diameter and those larger than 7 cm produced the highest percentage of positive smears. Cases with positive hilar and bronchopulmonary nodes yielded a higher percentage of positive bronchial washings than those with negative nodes. Sputum results remained much the same for the two groups.

Positive smears were obtained in 56.1% of operable cases and 59% of inoperable cases. With a positive biopsy, the number of operable cases decreased notably. In 59 operable cases, cytology was the only positive tissue diagnosis before operation. Thirteen frozen sections (with 11 positive) were asked for in these cases. Thus in 48 cases resection was done with cytology as the sole tissue diagnosis.

Typing of positive smears was 79.3% accurate. Epidermoid carcinomas were correctly typed in 89.2% of instances, undifferentiated carcinomas in 76.2% and adenocarcinomas in 39.3%. Two bronchiolar carcinomas were accurately typed from smears.

**Lung Cancer Death Rates among Nonsmokers and Pipe and Cigaret Smokers. Evaluation in Relation to Air Pollution by Benzpyrene and Other Substances.** By means of data from the first two years of study of environmental histories of persons with and without cancer being conducted by the Cheshire and North Wales Branch of the British Empire Cancer Campaign, Percy Stocks and John M. Campbell<sup>9</sup> (London) calculated death rates from cancer of the lung and bronchus among men of different smoking habits living

(9) Brit. M. J. 2:923-929 Oct. 15, 1955.

in a rural area of Wales, in a mixed area around Chester and Wrexham and in Liverpool county borough. Death rates were then related to measurements of benzpyrene and other substances present in the air within those areas.

Rural death rate increases proportionately to number of cigarettes smoked per week, and pipe smokers as a group rank with cigarette smokers of about 25 a week. Liverpool rates exceed rural rates in every smoking category, but urban-rural ratio falls progressively from about 9:1 among non-smokers to a small value approaching unity among heavy cigarette smokers. Absolute urban excess is much the same in each smoking group, suggesting that an "urban" factor is added to effects of smoking. Differences in smoking habits of the population can account for only a small fraction of contrast in total rates, and it is estimated that about half the Liverpool deaths of men from lung cancer arise from cigarette smoking and about three-fourths of the remaining half are due to a factor only slightly present in the rural area.

Concentration of smoke and of 3,4-benzpyrene, other polycyclic hydrocarbons and sulfur dioxide in the air rises with increasing urbanization, the benzpyrene figure in Liverpool being 8.11 times as great as in rural localities examined, a ratio which corresponds with estimated mortality ratio among non-smokers living in those areas. When death rates are compared with calculated total intake, by different categories of smokers in the areas of benzpyrene derived from air according to certain assumptions, plus that derived from number of cigarettes smoked, degree of correspondence is such as to suggest that benzpyrene might be the one agent involved.

The authors present this interim communication because a supposition that benzpyrene plays a dual part through cigarettes and air pollution now appears to be tenable, and such a working hypothesis may assist research work in this field, whether or not it is finally substantiated.

► [This is another bit of evidence to add to the many other studies that show the importance of cigarette smoking in the etiology of bronchial carcinoma. It is significant that no study yet reported indicates that cigarette smoking is of no importance.—Ed.]

**Is There No Increase of Lung Cancer in the Soviet Union?** The statement made by Amulree, in 1954, after a visit by British physicians to the Soviet Union that lung

cancer is not increasing there, despite the fact that many people "smoke like a chimney," is questioned by F. Lickint<sup>1</sup> on the basis of previously published data.

In 1918, Hampeln noted that in Riga, since 1895, there had been both absolute and relative increase in lung cancer in hospital and private practice and that many of these patients were "heavy drinkers and smokers." Uglov, from Leningrad, said in 1949 that since Derishanow's review covering 1901-29, lung cancer had steadily increased. From 1901 to 1920, lung cancer accounted for 0.17% of total operations, from 1921 to 1929, 1.8%. On the basis of 52,420 sections, Symons stated that in 1914 lung cancer amounted to 0.7%, in 1924, 1.6%, and in 1927, 2% of total deaths. In relation to cancer of other organs, the number of lung cancers had increased. Pajd showed that, in the last 20 years in the USSR, the actual number of lung cancers had increased from 2.3% to 11.8% of all cancers. According to Davidowski, primary lung cancer accounted for 12.5% of all cancer cases in 1929 and in men assumed second place (after cancer of the stomach). He stated that lung cancer seemed to be the only type malignancy that showed a definite increase and that increase in cancer deaths was mainly related to increase of bronchial cancer, one of the worst clinical types and most malignant, with 100% inoperability.

Perfiljew, in 1929, also reported from Russia that there had been an increase in lung cancer for 15-20 years, at a time when, in many German cities, increase in lung cancer had not yet begun. Preponderance in men was reported by Davidowski and by Lounkevitch (1938) who cited a 33:1 sex ratio.

At the recent 26th Congress of Surgeons of the USSR (1954), Kuprijanow, in reporting results of surgery in the last eight years, said that operations for removal of a lung or part of a lung for purulent lesions or lung tumors were performed by many general surgeons in outlying regions.

These reports would appear sufficient to deny the British statement, but it is interesting to seek its source. Last year it was widely published that at the last International Cancer Congress in São Paulo, it was reported that the attempt to develop nontoxic cigaret tobacco was already successful in the Soviet Union. It was assumed that Georgian, par-



ticularly Caucasian, tobacco differs significantly from American tobacco and contains little or no carcinogenic substance. Studies with the same methods of tobacco smears that have been done with other tobaccos are urgently needed. Lickint believes that such investigation would prove disappointing, since Roffo has already investigated tobaccos from Turkey, Egypt, Kentucky, Havana, Italy, Paraguay, Germany and other places and found but slight differences in cancerogenic effect. Such an effect was never completely lacking.

**Induction of Bronchial Cancer by Local Massive Carcinogen Concentrate in Outdrifting Mucus** is discussed by Charles C. Macklin<sup>2</sup> (Univ. of Toronto). Inhalation of cigaret smoke causes the small particles in the smoke to be carried to the rich capillary net of the delicate alveolar walls where the diffusible product is immediately absorbed. Some of the tarry ultramicroscopic materials remain on the alveolar walls, undoubtedly temporarily entrapped in the alveolar mucoid fluid, and are speedily accumulated in the segregation apparatus of the phagocytic pneumonocytes.

These dust cells make their way to the glottis to be swallowed or spat out. Only a fraction of the dust cells reach the glottis intact, most disintegrate and their contents are borne along in the raft of mucus that constantly moves from the alveolar region along the bronchial system to the trachea and glottis. This raft is motivated by millions of underlying ciliary fingers waving outward. The mucus raft is loaded with the carcinogenic smoke derivatives. Its route is shown in Figure 27.

As the raft moves from the alveolar walls to the hilar area the various streams of mucus converge and the carcinogenic substances become concentrated. The peripheral alveolar zone acts as the main catchment basin of the smoke-carried carcinogens. The converging currents of mucus reach the vulnerable hilar epithelium. The pathway includes the alveolar bronchioles, transitional bronchioles, various orders of smooth-walled bronchioles and the small, medium and large bronchi. In the larger bronchi of the hilar region the carcinogens are tremendously concentrated. The epithelial cells of the large bronchi, underneath the mucus raft, are exposed more than those of any other part of the

bronchial tree to the delinquency-promoting action of carcinogens on cells, explaining why most bronchial carcinoma develops in the hilar region.

A slowing at confluences in the hilar region also contributes to development of carcinoma in this region. At the great bronchial confluences, much of the mucus current

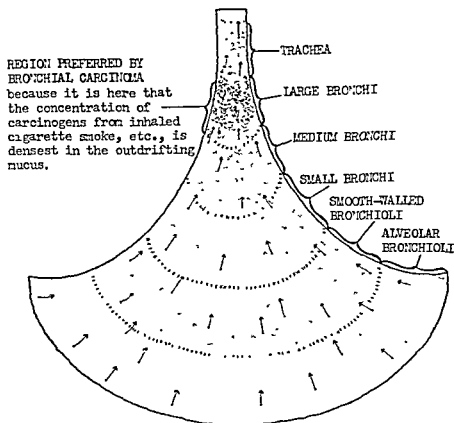


FIG. 27. "C. C. Macklin" diagram illustrating concept of surface drainage field of in- of raft of mucus, dots indicate carcinogens transverse crescentic lines indicate carinae are marked off for alveolated bronchiole bronchiole and the small, medium and large orational basis (Courtesy of Macklin, C. C.: 1956)

shifts laterally, entailing thickening of the mass at such points and delay in its onward progress, causing extra accumulation and lingering of the mucus. Ciliary paralysis, partial or complete, also acts as an accessory retarding influence. Metaplastic change even removes the cilia. In the hilar region of the bronchial tree, there is more cancer-producing substance acting on the epithelium for a longer time than anywhere else in the air tract.

The effective carcinogenous material is probably not in-

tracellular. More likely it is in the remains of phagocytes which carry it out of the alveoli and along the alveolar bronchiole to the ciliated part of the air tract. Some of the material may never be phagocytized at all but may be intercepted as particles by the sticky mucus of the raft. Doubtless the carcinogen acts as a molecular solution upon the epithelium. Carcinogenic power probably varies directly with the concentration. Smog particles and radioactive dust are also trapped in the alveoli and concentrated in the hilar region in the same manner as cigaret smoke.

Prevention of lung cancer entails total abstinence from cigarettes. Short of this it is wise to exercise moderation and particularly to abstain from inhaling the smoke.

► [The brilliant conception of Dr. Macklin explains satisfactorily what heretofore could not be adequately explained, namely, the reason for the frequent location of bronchogenic carcinoma in the large bronchi but almost never in the trachea.—Ed.]

**Distribution and Absorption of Tobacco Tar in Organs of Respiratory Tract** were studied by Pentti Grimala and Lars R. Holsti<sup>3</sup> (Univ. of Helsinki). For the former, a full scale plaster model of the human organs lined with a layer of egg white to simulate mucosa was used. The absorption experiments were done on mice, guinea pigs and one monkey.

It was found that localization of tobacco smoke is conditioned mechanically by the course of smoke in the respiratory tract. Adherence of substances on the mucous lining is a passive phenomenon. Distribution of tar in the different regions varies greatly according to the type of smoking (pipe, cigaret). Tar distribution in the plaster model after smoking 5 Gm. of cigaret tobacco (Fig. 28) corresponded closely with the sites of predilection of cancer in the respiratory tract (Fig. 29).

The combustion process is partly oxidation and partly dry distillation. The quality and quantity of decomposition products depend on the rate and temperature of the process, water content of the tobacco and amount of air passing through the tobacco. Relatively more tar is seen in the lower respiratory tract in cigaret than in pipe smoking.

The heaviest localization generally occurred at the sites of contact of the most concentrated smoke, such as the lips, mobile portion of the tongue and the mucosa of the cheeks between the rows of teeth. Deeper in the respiratory tract

(3) Cancer 8:673-678, July-Aug., 1955.

tar mainly became localized in the narrow portions, where the smoke stream strikes the walls of the organs, i.e., tonsillar region, vocal cords and tracheal and bronchial bifurcations. Only very small amounts were seen on the hard palate and trachea. Nor is smoke brought to bear directly on the dorsal wall of the pharynx, as its direction is changed by gyratory motions occurring in the buccal cavity during suction with the cheeks. In addition to quantitative vari-

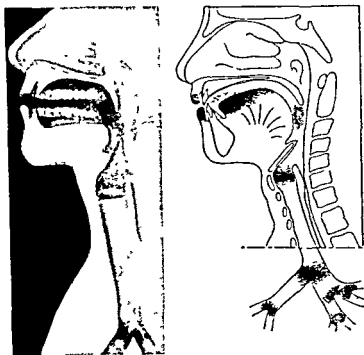


Fig 28 (left) —Distribution of tobacco tar in plaster model of human organs after smoking of cigaret

Fig 29 (right) —Clinical frequency of cancer of respiratory tract

(Courtesy of Ermala, P, and Holsti, L R Cancer 8 673 678, July Aug, 1955)

ations in the localization of tobacco tar, marked qualitative differences may be seen, i.e., fractionation of tar in different regions. In pipe smoking most of the tar condenses as early as the anterior part of the buccal cavity. Of the fraction distilled at a higher temperature, only a relatively small part, compared with cigaret smoking, reaches the lungs.

Penetration of tobacco tar into the cells and tissues is not so much due to the amount of tar on the tissue surface as to absorptive properties of the tissue itself. Some organs absorb only small quantities of tar even from a large amount present on the surface. Absorption of fat-soluble substances through intact skin is possible (1) through the appendages

tracellular. More likely it is in the remains of phagocyte which carry it out of the alveoli and along the alveolar bronchioles to the ciliated part of the air tract. Some of the material may never be phagocytized at all but may be intercepted as particles by the sticky mucus of the raft. Doubtless the carcinogen acts as a molecular solution upon the epithelium. Carcinogenic power probably varies directly with the concentration. Smog particles and radioactive dust are also trapped in the alveoli and concentrated in the hilar region in the same manner as cigaret smoke.

Prevention of lung cancer entails total abstinence from cigarettes. Short of this it is wise to exercise moderation and particularly to abstain from inhaling the smoke.

► [The brilliant conception of Dr. Macklin explains satisfactorily what heretofore could not be adequately explained, namely, the reason for the frequent location of bronchogenic carcinoma in the large bronchi but almost never in the trachea.—Ed.]

**Distribution and Absorption of Tobacco Tar in Organs of Respiratory Tract** were studied by Pentti Ermala and Lar R. Holm (Univ. of Helsinki). For the former a full scale plaster model of the human organs lined with a layer of egg white to simulate mucosa was used. The absorption experiments were done on mice, guinea pigs and one monkey.

It was found that localization of tobacco smoke is conditioned mechanically by the course of smoke in the respiratory tract. Adherence of substances on the mucous lining is a passive phenomenon. Distribution of tar in the different regions varies greatly according to the type of smoking (pipe, cigaret). Tar distribution in the plaster model after smoking 5 Gm. of cigaret tobacco (Fig. 28) corresponded closely with the sites of predilection of cancer in the respiratory tract (Fig. 29).

The combustion process is partly oxidation and partly dry distillation. The quality and quantity of decomposition products depend on the rate and temperature of the process, water content of the tobacco and amount of air passing through the tobacco. Relatively more tar is seen in the lower respiratory tract in cigaret than in pipe smoking.

The heaviest localization generally occurred at the site of contact of the most concentrated smoke such as the lip-mobile portion of the tongue and the mucosa of the cheek between the rows of teeth. Deeper in the respiratory tract

mainly became localized in the narrow portions, where smoke stream strikes the walls of the organs, i.e., tonsil-region, vocal cords and tracheal and bronchial bifurcations. Only very small amounts were seen on the hard palate and trachea. Nor is smoke brought to bear directly on the dorsal wall of the pharynx, as its direction is changed by gyratory motions occurring in the buccal cavity during suction with the cheeks. In addition to quantitative variation

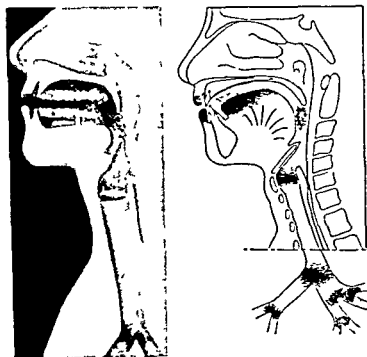


Fig. 28 (left) —Distribution of tobacco tar in plaster model of human organs after smoking of cigaret

Fig. 29 (right) —Clinical frequency of cancer of respiratory tract

Courtesy of Ermala, P, and Holsti, L R Cancer 8 673 678, July Aug, 1955 )

differences in the localization of tobacco tar, marked qualitative differences may be seen, i.e., fractionation of tar in different regions. In pipe smoking most of the tar condenses as early as the anterior part of the buccal cavity. Of the fraction dislodged at a higher temperature, only a relatively small part, compared with cigaret smoking, reaches the lungs.

Penetration of tobacco tar into the cells and tissues is not so much due to the amount of tar on the tissue surface as to absorptive properties of the tissue itself. Some organs absorb only small quantities of tar even from a large amount present on the surface. Absorption of fat-soluble substances through intact skin is possible (1) through the appendages

or (2) directly percutaneously (Fig. 32). Penetration of tobacco tar through the skin of the lips occurs by both mechanisms. The hair shaft does not adhere to the follicular wall—there is a space between, loosely filled with greasy, horny scales and hair. Tobacco tar swabbed on the skin soon penetrates this space and reaches sebaceous glands, which are capable of accumulating great amounts of fluorescent tar (Figs. 30 and 31). From there it easily enters surrounding tissues and the blood stream. Subcutaneous fat



Fig. 30—Lower lip of monkey (Courtesy of Ermala, P, and Holsti, L. R. *Cancer* 8 673-678, July-Aug., 1955)

fluoresces strongly within a few minutes after administration of tar on the skin surface, and the fluorescence in the sebaceous elements and fat can be seen clearly at least five hours later. True percutaneous absorption through the intact epidermis occurs much more slowly. Appendages are absent in the oral cavity and upper respiratory tract, which are covered with stratified epithelium. Intake of substances is therefore possible only by penetration of the epidermis. The ciliated epithelium of the deeper respiratory tracts is capable of absorbing only negligible amounts of tar, with no perceptible differences between various regions. Localization of the action of tobacco tar thus corresponds with the passive distribution in the plaster model, except for tissues containing subcutaneous fat.

Experience with chemical carcinogens shows that long and intensive local action on tissue is usually required. Besides surface distribution and actual absorption, storage of the agent in tissues is significant. Different lipid accumulations are the tissue constituents actually capable of storage.

A striking correlation is noted between the clinical frequency of cancer and localization of tobacco smoke, espe-

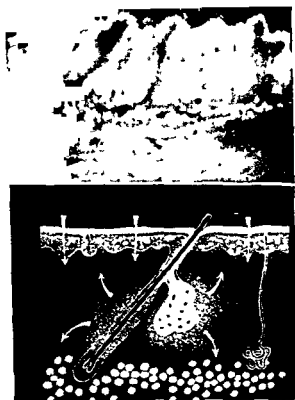


Fig. 31 (top).—Section of skin of lower lip of mouse swabbed with tobacco tar (ultraviolet light photograph)

Fig. 32 (bottom).—Mechanism of percutaneous absorption of tobacco tar (Compare with Figure 31)

(Courtesy of Ermala, P., and Holsti, L. R. *Cancer* 8 673-678, July-Aug., 1955)

cially in view of smoking habits. About 15-20% of all carcinomas occur in the respiratory tract. For pulmonary cancer, the figure is 10-15%. In pipe smoking, the effect of tar strikes mainly on the anterior part of the buccal cavity, where fractions of tobacco with even a high boiling point become condensed. In cigaret smoking, a great amount of tar reaches as far down as the lungs. Inhalation is much more common among cigaret smokers, a noteworthy factor, especially in view of sex incidence. Bronchogenic cancer usually originates in the main bronchial bifurcation, where tar tends to accumulate.



or (2) directly percutaneously (Fig. 32). Penetration of tobacco tar through the skin of the lips occurs by both mechanisms. The hair shaft does not adhere to the follicular wall—there is a space between, loosely filled with greasy, horny scales and hair. Tobacco tar swabbed on the skin soon penetrates this space and reaches sebaceous glands, which are capable of accumulating great amounts of fluorescent tar (Figs. 30 and 31). From there it easily enters surrounding tissues and the blood stream. Subcutaneous fat



Fig. 30—Lower lip of monkey (Courtesy of Ermala, P., and Holsti, L. R. • Cancer 8 673 678, July Aug, 1955)

fluoresces strongly within a few minutes after administration of tar on the skin surface, and the fluorescence in the sebaceous elements and fat can be seen clearly at least five hours later. True percutaneous absorption through the intact epidermis occurs much more slowly. Appendages are absent in the oral cavity and upper respiratory tract, which are covered with stratified epithelium. Intake of substances is therefore possible only by penetration of the epidermis. The ciliated epithelium of the deeper respiratory tracts is capable of absorbing only negligible amounts of tar, with no perceptible differences between various regions. Localization of the action of tobacco tar thus corresponds with the passive distribution in the plaster model, except for tissues containing subcutaneous fat

Experience with chemical carcinogens shows that long and intensive local action on tissue is usually required. Besides surface distribution and actual absorption, storage of the agent in tissues is significant. Different lipid accumulations are the tissue constituents actually capable of storage.

A striking correlation is noted between the clinical frequency of cancer and localization of tobacco smoke, espe-

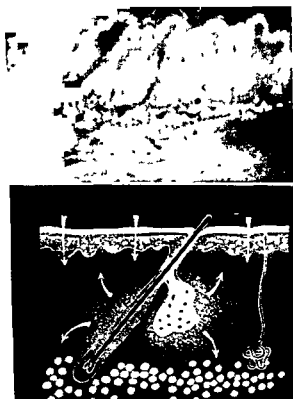


Fig 31 (top) —Section of skin of lower lip of mouse swabbed with tobacco tar (ultraviolet light photograph)

Fig 32 (bottom) —Mechanism of percutaneous absorption of tobacco tar (Compare with Figure 31)

(Courtesy of Ernala, P, and Holsti, L. R. Cancer 8 673 678, July Aug, 1955)

cially in view of smoking habits. About 15-20% of all carcinomas occur in the respiratory tract. For pulmonary cancer, the figure is 10-15%. In pipe smoking, the effect of tar strikes mainly on the anterior part of the buccal cavity, where fractions of tobacco with even a high boiling point become condensed. In cigaret smoking, a great amount of tar reaches as far down as the lungs. Inhalation is much more common among cigaret smokers. a noteworthy factor, especially in view of sex incidence. Bronchogenic cancer usually originates in the main bronchial bifurcation, where tar tends to accumulate.

The correlation between the clinical incidence of cancer and localization of tobacco tar may be considered additional support, though not conclusive, for the theory that tobacco may have some significance as a carcinogenic agent

**Examination of Results of Surgical Treatment of Cancer of the Lung** by M Berard, E C Saubier and G Maret<sup>4</sup> showed 15 deaths (28%) after 53 resections performed during 1948-51, and only 4 (7%) after 55 resections during 1952-54 In the first series, nine deaths occurred at conclusion of operation or immediately afterward, and only one was due to surgical accident There were two instances of cardiac arrest, and six failures to recover from anesthesia, one after diffuse hemorrhage and transfusion Of six deaths that occurred 8-48 hours after operation, two were due to pulmonary embolism, one patient each had fever and symptoms of heart failure, confusion on emergence from anesthesia, progressive pulmonary edema and paralytic ileus

These patients were operated on under deep anesthesia with nesdonal, curare and oxygen, with controlled respiration Later, use of curare was greatly reduced, and light anesthesia, elimination of controlled respiration and immediate awakening after operation not only reduced the risk of operation but modified its after-effects, e g, paralytic ileus disappeared completely Three of four deaths among 55 patients in the later series were due to unavoidable surgical accidents the other was in an aged poor-risk patient Prompt use of heparin and dicumarol,<sup>®</sup> when indicated, reduced thrombosis and embolism to a minimum

Among 108 patients who had pulmonary resections in 1948-54, 37 were still living Three were alive and well more than five years, one more than four years, four over three years, four over two years and seven over one year In almost all patients whose survival was prolonged, histologic diagnosis was epidermoid carcinoma No cure of long duration was observed in small cell carcinoma In tumors of the same histologic type, size and local extension are not prognostically significant

Decision as to operability of a tumor should, in borderline cases, depend on histologic diagnosis, angiocardigraphic findings (amputation of the vena cava at the entrance to the auricle indicates adenopathy which precludes operation)

(4) Lyon chir 50 534-546, July 1955

and laterality (right pneumonectomy is always more serious). If exploratory thoracotomy is done, pulmonary cancer should not be judged inoperable without opening the pericardium. In some cases artery and pulmonary veins can be ligated satisfactorily to free the main stem bronchus all the way to the trachea and to remove lung tumor and surrounding lymph nodes en bloc. Neoplastic invasion of the superior vena cava and extension of tumor to the opposite bronchus represent insurmountable obstacles to satisfactory resection.

Question of whether to do pneumonectomy or lobectomy arises in the case of a circumscribed peripheral tumor that leaves the pedicle of the lobe free from local extension or adenopathy. Such a lesion should be treated by lobectomy in the aged patient. If pneumonectomy is decided on for a small lesion, choice then must be made between simple or radical pneumonectomy. Since radical pneumonectomy carries no higher immediate risk than simple pneumonectomy, it seems logical to extend the operation. In their last 50 pneumonectomies, the authors used the intrapericardial approach in 42, but final evaluation of results cannot yet be made.

► [These results are very commendable. There is no definite answer to the question of whether pneumonectomy gives better results than lobectomy or vice versa. Perhaps there never will be because except in a very large series with comparable conditions the figures will not be statistically significant. My first patient with successful pneumonectomy for carcinoma is still living and well more than 23 years later.—Ed.]

**Surgical Treatment of Lung Cancer in Copenhagen.** Results in Geographic Section of Population are reported by Jens L. Hansen, Thue Poulsen and Hans Rahbek Sørensen<sup>5</sup> (Univ. of Copenhagen). In a population of about a million, incidence of lung cancer rose from 112 in 1943 to 294 in 1952 and percentage of operated patients from 13.6 in 1943-44 to 30.8 in 1951-52. During this period, the percentage of patients surviving resection increased from 2.3 to 20.9. Owing to the great increase in diagnosed cases the absolute number of patients not operated on increased from 94 in 1943 to 187 in 1952. During the first years, most operations were exploratory thoracotomies. Resections constituted only about 30% of operations in early years, whereas in recent years they constituted about 70%. Operative mor-

tality dropped from almost 50% in early years to about 20% in recent years

Follow up showed that of 89 patients with pulmonary resections, 31.1% were still living at the end of five years. Of these survivors, one died 7 and one 11 years postoperatively, others were living 5-11 years postoperatively. Five year survival among 572 patients seen from 1943 to 1946 was 1%, among 403 patients seen from 1947 to 1948, 3%, and among 194 patients seen in 1949, 4.5%. In 1952, 21.8% of all patients were discharged following resection. If this group can be expected to show a survival rate of 30%, the five year survival for all patients will have increased from about 1% in 1943 to 6.5% in 1952.

The great progress made in surgical treatment of lung cancer is due mainly to better and earlier diagnosis.

**Combined Radiotherapy and Resection for Carcinoma of Bronchus: Experiences with 66 Patients.** L. L. Bromley and Leon Szur<sup>6</sup> (Hammersmith Hosp., London) administered an average of 4,700 r to 66 patients with bronchial carcinoma during an average of six weeks. Some of the tumors were inoperable because of the site. Despite radiotherapy, surgery was not complicated except for more than usual fibrous tissue around the hilar structures during the resection. There was squamous cell carcinoma in 42, oat cell carcinoma in 11, adenocarcinoma in 3 and other types in 10. The removed specimens, after preoperative irradiation, revealed tumor to be absent in 29, present but degenerate in 14 and present and viable in 19, the specimen was lost in 4. Of the 66 patients 10 died postoperatively, 38 died with cancer, 5 died of intercurrent disease, 2 are alive with cancer and 11 are alive without cancer. Of the living patients, two are alive after five years or more, three after four years, five after three years and three after two years. Survival times of 38 patients who died with cancer were under one year in 21, one to two years in 11, two to three years in 4 and over four years in 2.

None of the patients with oat cell or adenocarcinoma cancers are alive whereas 9 of 42 with squamous cell carcinoma are alive. Of 24 patients originally considered operable with no tumor present in the resected specimen, 6 are alive, of 11 with degenerate tumor present, 2 are alive, of 14 with

viable tumor present, 2 are alive, and of 3 whose specimens were lost, 1 is alive. None of the patients with tumors originally considered only technically operable or nonoperable are alive.

The method of treatment has not produced impressive results. The survival rate was not high, and although almost half the tumors were eradicated by the irradiation the incidence of empyema (5 cases) and fistula (13 cases) was high. The constitutional effects of irradiation were slight and the general condition of many patients improved considerably. Irradiation seemed to convert some patients from the inoperable to the operable group.

Intrapericardial Dissection in Right Pneumonectomy for Bronchogenic Carcinoma is described by William H. Wier-

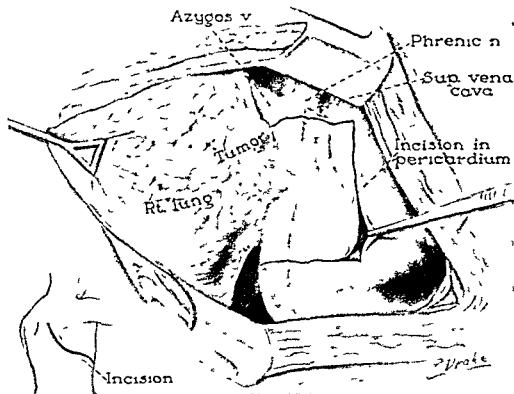


Fig 33 (Courtesy of Wierman, W. H., et al J Thoracic Surg 30 76 80, July, 1955)

man, John W. Kirklin and F. Henry Ellis, Jr.<sup>7</sup> (Mayo Clinic and Found.).

**TECHNIC.**—A posterolateral incision is made through the 5th interspace or bed of the resected 6th rib. Incision of mediastinal pleura over the azygous vein is carried down anteriorly across the superior

(7) J Thoracic Surg 30 76 80, July, 1955

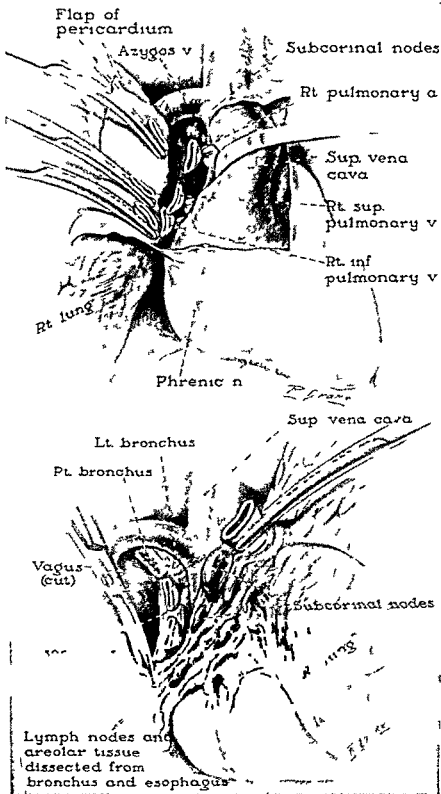


Fig 34 (top)

Fig 35 (bottom)

(Courtesy of Wierman W H *et al* J Thorac Surg 30 76 80 J ly 1955)

vena cava and the pericardium is opened longitudinally just behind the phrenic nerve. When carcinoma encroaches on the pericardium anteriorly, the latter must be opened anterior to the phrenic nerve (Fig. 33). Superior and inferior pulmonary veins are secured first when possible, the former being doubly ligated on the proximal side flush with posterior wall of left atrium and divided. The inferior pulmonary vein is generally secured within the pericardium. The pulmonary artery is freed beneath the retracted superior vena cava where it is doubly ligated on the proximal side and divided (Fig. 34). The lung is then retracted anteriorly and the incision of the mediastinal pleura is carried down over the esophagus. The right main bronchus is dissected out so that subcortical lymph nodes and nodes along proximal reaches of the left main bronchus are peeled down with the specimen. Lymph nodes lying along the adjacent esophagus are dissected up to be removed en bloc with lung and soft tissue and remainder of mediastinal lymph nodes. The bronchus is cut across flush with the trachea and closed with interrupted silk. The vagus nerve is severed as it emerges from beneath the azygos vein and a portion of it removed. A portion of pericardium and soft tissue in this region is likewise dissected away (Fig. 35). When resection is completed, defects remain in the pericardium and mediastinal pleura in the hilar region. The left main bronchus, esophagus and aorta can all be seen. The bronchial stump is carefully covered with mediastinal pleura and soft tissue. The thoracic wall is closed in layers without drainage.

Right pneumonectomy with intrapericardial dissection has been done in 32 cases and left pneumonectomy with intrapericardial dissection in 49. Among the 81 patients there were six hospital deaths (7.4%), two after left and four after right pneumonectomy (12.5%). Two of these last four deaths resulted from respiratory insufficiency in the late postoperative period, one was due to massive embolus to the left pulmonary artery and one to empyema and bronchopleural fistula. Only in the last case could the more radical pneumonectomy have been possibly implicated in the death, but the clinical impression was that the bronchopleural fistula was perhaps secondary to empyema.

Whether this aggressive mode of attack on bronchogenic carcinoma has a more favorable effect on survival rate than standard pneumonectomy remains to be determined.

**Radical Pneumonectomy for Bronchial Carcinoma** is reported by Russell Brock and L. L. Whytehead<sup>8</sup>. The operation conforms to generally accepted principles of cancer surgery, viz., removal of the affected organ, its fascial connections and lymphatic field in one block. Routinely securing

(8) Brit J Surg 43:824 July 1955



the pulmonary artery and vein at their origin within the pericardium is important because a common mode of spread of carcinoma is along these vessels, therefore, the hilar compartment should not be touched at operation, and intra-pericardial ligation should always be done with resection of an oval of pericardium surrounding the hilar structures.

Since the operation was designed and first performed in June 1947, 145 radical procedures and 49 simple pneumonectomies for carcinoma have been done by the same surgical group. Operative mortality of radical pneumonectomy was 11% (16 deaths) and of simple pneumonectomy 18% (9 deaths), showing that the radical operation is not more dangerous than lesser procedures. Of 31 patients having simple pneumonectomy who died later, 1 lived over seven years, 1 over three years and 2 over two years, 27 died within two years. Of the nine surviving (18%), five were living over five years later, one over six years and three over eight years. Of 57 patients who died since radical pneumonectomy, 46 died within two years after operation, of the others 1 lived over five years, 1 over four years, 2 over three years and 7 over two years. Of the 72 surviving (50%), 15 were living five to over seven years later and 20 three to over four years later.

Lymphatic nodes were invaded with growth in all long-survival patients. In those with shorter survival, incidence of nodes involved with growth and free from growth was approximately equal, suggesting that blood-borne metastases and inherent malignancy of the process were responsible for death.

Deep x-ray therapy was used in only a few patients after pneumonectomy when it seemed improper to withhold possible additional benefits that deep irradiation may offer. In a woman, aged 28, a large inoperable oat-celled carcinoma of the right upper lobe was treated by deep x-ray therapy which reduced the lesion so that operation was performed six months later. The primary growth appeared yellowish and necrotic after removal, and several excised nodes contained similar necrotic tissue; none showed active growth. She was living and well six years after operation.

Radical pneumonectomy is in theory, a sound operation for bronchial carcinoma; has proved satisfactory in practice over eight years and yields a higher percentage of cures.

Cancer Cells in the Sputum were reported long before Papanicolaou's work stimulated the widespread current interest in cytologic diagnosis, according to Norah Schuster<sup>9</sup> In 1860, W H Walshe reported that "encephaloid debris has on rare occasions been expectorated, and cancer cells have occasionally been found microscopically where the naked eye characters have failed to appear" In 1886, Francis Troup mentioned that morsels of tissue may be expectorated which can be recognized as malignant Hampeln of Riga began a microscopic study of sputum in 1897 and by 1919 had collected 13 examples of neoplastic cells from 25 cases of pulmonary cancer In 1898, Lenhartz described a combination of large abnormal epithelial cells with fatty cells as suggestive of lung cancer, though he did not claim that they were actually malignant cells Betschart, in 1895, cited only three examples in an article on the diagnosis of malignant pulmonary tumors from the sputum In 1929, at the Royal Chest Hospital (London), it became regular practice to examine fresh wet-stained films of sputum, and clustered or isolated malignant cells were often found, sometimes unexpectedly Dudgeon and Wrigley's paper on fixed films, in 1935, gave impetus to search for malignant cells in sputum Papanicolaou described a more elaborate stain for fixed films which has been extensively applied In South America and France the usual custom is to make serial sections of the whole sputum In Russia, Althausen worked with fresh films Each method has its merits and drawbacks, and each pathologist his own preference

In wet preparations, cells are seen in the round and malignant ones often are striking, with their exuberant size and deformity, their phagocytic power and signs of degeneration The search for malignant features is often concentrated on the nucleus, but the neoplastic cell body is irregularly shaped and lipid change is characteristic

Recognition of malignant cells in sputum of patients with pulmonary cancer varies from 60 to 80% The sputum may point to a neoplasm when other signs are inconclusive It sometimes reveals a neoplasm coexisting with another known lesion, such as tuberculosis Diagnostically, sputum smears compare favorably with bronchoscopy In one series

(9) Tubercle 36 350 355 November 1955

of patients with pulmonary carcinoma 50% had bronchoscopic signs and 53% had malignant cells in the sputum. When both methods were used, correct diagnoses rose to 92%. The methods are complementary, since bronchoscopy fails to reveal peripheral lesions and sputum examination is valueless in nonulcerative lesions. About 2% false positives are inevitable, because of the cell proliferation and metaplasia that occurs with old or chronic inflammation.

In view of the favorable response of large or squamous cell tumors to surgery, it is fortunate that they frequently soften and discharge into bronchi and that their malignant cells are probably the least difficult to recognize. Their identification in sputum might be a deciding factor for excision. Sputum cytology of secondary neoplasms cannot be distinguished from that of primary unless some peculiar formation gives a clue. In general, cancer cells are sufficiently recognizable in sputum to be accepted as a diagnostic aid that should not be neglected.

► [In the list of those named by the author as preceding Papanicolaou in the examination of the sputum in bronchogenic carcinoma certainly the name of H. H. Wandall of Copenhagen should be included. In 1944 he published what was up to that time the largest study of this question (*Acta chir. scandinav.* (supp. 93) 91:1, 1944). While spending a year with us in 1944 at the Barnes Hospital he was successful in making better than a 90% record of correct diagnosis in 100 cases of lung cancer. There can no longer be any doubt about the diagnostic value of sputum examinations in cases of suspected bronchogenic carcinoma.—Ed.]

**Significance of Histologic Types in Diagnosis and Prognosis of Bronchogenic Carcinoma** was evaluated by Gudmund Toft<sup>1</sup> (Copenhagen) in a study of 355 cases. There were 236 squamous, 98 anaplastic and 21 adenomatous carcinomas. Male:female sex ratio for the entire group was 11:3:1 and for those with squamous carcinoma 15:9:1. Average age was 57.2 years. All types of tumors were situated most often in an upper lobe. Those with undifferentiated carcinoma had symptoms of shortest duration.

A preoperative microscopic diagnosis of cancer was obtained with certainty in 60% of cases by bronchoscopy-biopsy and cytologic examinations of bronchial secretion and sputum and cancer was suspected but not proved in another 22%. Diagnosis was more certain in squamous and anaplastic carcinomas than with adenomas, which are more often peripherally situated. Operations were possible in

(1) *Acta path. et microbiol. scandinav.* (supp. 103) pp. 219-236, 1955.

73.8% and resections were carried out in 56.3%. Among those with squamous carcinomas, 77.5% were operable and 61% were resected, for those with undifferentiated carcinomas, 62.2% and 59%, and for those with adenomas, 86% and 86%, respectively. Average survival of those not treated surgically was six months for squamous carcinoma and two months for anaplastic carcinoma. For those who underwent thoracotomy average survival for squamous carcinoma was 7.8 months and for anaplastic carcinoma 2.7 months. Of patients with squamous carcinomas who had resections, approximately 24% survived over five years. For those who died average survival was 10.4 months. None of the patients with anaplastic carcinomas lived for five years. One was alive 3 years after operation, and average survival after resection was 8.2 months. Among those with adenomas one patient (of two) lived five years after operation one (of seven) three years. Average survival of resected patients who died was 14.7 months.

Cancer was not detected in regional lymph nodes in any patient who lived over three years. Average survival of those with squamous carcinomas on whom resections were performed and who died later was about three months shorter when cancer had been detected in lymph nodes. This difference was not apparent in cases of undifferentiated carcinomas. Hence anaplastic carcinomas have a far poorer prognosis than squamous or adenomatous lesions. Surgery is of doubtful value in anaplastic lung carcinomas, but since the preoperative pathologic diagnosis sometimes must be revised when the entire tumor is examined histologically all cancers of the lung should be operated on provided they otherwise meet the criteria for operability.

**Cell Types and Histologic Patterns in Carcinoma of Lung.** Observations on Significance of Tumors Containing More Than One Type of Cell are reported by Charles T. Olcott<sup>2</sup> (New York Hosp. Cornell Med. Center). Histologic study was made of 234 cases of carcinoma of the lungs and bronchi seen between 1925 and 1953.

Cells found in carcinomas were of four types: large polygonal, small round, epidermoid and columnar, the last including adenocarcinoma and terminal bronchiolar carci-

noma. Tumors composed exclusively of one of these four types of cells made up 65% of the cases; growths containing mixtures of two or three types of cells were found in the rest.

The large polygonal cells seemed to merge with small round cells, especially when they were found at the periphery of a mass of cells that contained the smaller cells near the center. Furthermore, the large polygonal cells sometimes were found alone in metastases from a primary tumor that contained both large polygonal and small round cells. Hence the possibility was considered that the large polygonal cells might often be transformed into small round cells. In several instances, moreover, large polygonal cells were found in close apposition to epidermoid or columnar cells, or both, the findings suggesting that the large polygonal cells may also give rise to epidermoid or columnar cells.

In view of mixtures of cells found in a large proportion of growths and apparent differentiation of large polygonal cells into cells of other types, carcinoma of the lung, although obviously presenting various histologic pictures, should be regarded as a single entity. Findings are best explained on the assumption that large polygonal cells are the primary element in pulmonary carcinoma and that they may persist as such or become modified to form cancers composed of small round cells, epidermoid cells or columnar cells.

► [The editor cannot agree with Dr. Olcott's conclusions. For example, adenocarcinoma has many clinical features that distinguish it from epidermoid cancer. It is much less common than epidermoid, it has about an equal distribution between the two sexes, and it sometimes occurs at a much younger age than the epidermoid. Indeed a primary cancer of the lung that occurs before the age of 35 years is almost certain to be an adenocarcinoma. Those rare lung cancers that have been found in children have all been adenocarcinomas. Moreover, there is no demonstrable etiologic relationship to cigaret smoking in the case of an adenocarcinoma. In most instances of lung cancer in nonsmokers the tumor will be found to be an adenocarcinoma. The evidence, therefore, seems contradictory to the idea that carcinoma of the lung is a single entity. Again, the variety of primary carcinoma of the lung commonly called "alveolar cell carcinoma" is not at all like the types more frequently seen and there is some evidence that it originates in a virus infection.—Ed.]

Critical Comparison of Bronchoscopy, Bronchography and Angiopneumography in Bronchial Carcinoma was made in 25 cases by H. J. Hoffheim<sup>3</sup> (Univ. of Hamburg). The

(3) *Thoraxchirurgie* 3:139-150, August, 1955

following types of cases are considered inoperable (1) If bronchoscope reveals carcinoma in a main stem bronchus or if the carina, trachea or bronchi of the opposite side show changes (2) If the bronchogram shows obstruction or distortion of the main stem bronchus or narrowing of the tracheal wall of the bifurcation or of the opposite main stem bronchus, if the carina is distorted by metastatic lymph nodes or if the bifurcation is immobile, operability is questionable (3) If the angiogram shows total or partial vascular obstruction of a pulmonary artery, obstruction at the exit of a lobe artery makes operability questionable

Diagnosis of bronchial carcinoma could be established in all patients by angiopneumography alone. Among 21 patients, carcinoma was revealed by bronchography in all but 2. Bronchoscopy was least reliable, among 19 patients, carcinoma was demonstrated in only 13. Inoperability was indicated by angiography in 10 of 25 patients, by bronchography in 1 of 21 and by bronchoscopy in 1 of 19. Only one tumor that appeared inoperable in the angiopneumogram was amenable to resection. That inoperability was seldom proved by bronchography and bronchoscopy was largely due to deliberate choice of clinical material. Arterial studies were carried out principally on patients in whom bronchographic and bronchoscopic findings had not revealed inoperability.

Superiority of angiopneumography as a diagnostic method rests on the following facts. As in bronchography, pathologic changes are recorded on film and thus can be studied by more than one observer. Even more important, carcinomatous changes in lung parenchyma, even at the periphery, are revealed by angiography and the contrast medium delineates the entire tumor mass, whereas with the other methods, only the point of outgrowth of a malignant tumor into the bronchi can be localized. In the two patients in whom bronchography yielded no positive findings, carcinomatous changes in the bronchial tree were so slight that they could not be visualized by this method even though the tumor had already infiltrated widely into the lung tissue as was demonstrated on the angiogram.

**Thoracic Angiography in Bronchial Carcinoma** Josef Krall<sup>4</sup> (Univ. of Hamburg) reports on 50 venograms and

(4) Thoraxchirurgie 3:121-138, August 1955.

25 pneumoangiograms in proved cases. Usually, the indirect method, with injection of contrast medium through a heart catheter, was employed. The direct method (injection into an arm vein) was used only when cinematographic study was done. Various vascular changes accompanying bronchial carcinoma were demonstrated and compared with surgical and histopathologic findings. Certain angiographic signs were shown to furnish criteria of inoperability.

Definite signs of inoperability are injury and stenosis in the region of a lung artery (right or left main branch) and invasion by the tumor of the region of the superior vena cava. Similar changes in arteries of the lobes do not constitute overwhelming contraindications to pneumonectomy but create increased technical difficulties in the probably still feasible pulmonary resection. Besides these valuable prognostic signs thoracic angiography definitely aids in differential diagnosis of benign and malignant tumors and of bronchial carcinoma and inflammatory disease of the lungs and in localization of tumors i.e. whether they arise from the lung or mediastinum.

Thoracic angiography in bronchial carcinoma affords a visualization of spatial relation of the tumor to the vascular system of the superior vena cava and pulmonary artery. Knowledge of involvement of blood vessels by the tumor or its metastases may be important in determining whether or not operation is advisable and in prognosis.

**Bronchogenic Carcinoma. Autopsy Material from Non specialized Departments in Copenhagen City Hospital 1948**  
54 analyzed by Otto Gottlieb<sup>5</sup> yielded 145 cases (112 males). Average age of males was 58.6 and of females 60.5. Histologic examination in 124 cases showed undifferentiated carcinoma in 74, squamous cell in 38 and adenocarcinoma in 12. Duration of disease averaged 7.8 months for entire series but only 6.5 months for patients with anaplastic carcinoma. A relatively large proportion of undifferentiated lesions are not diagnosed until they have reached an inoperable stage. Squamous cell carcinoma of slower development is more likely to be diagnosed and to be referred for thoracic surgery. Forty cases (27%) were diagnosed post mortem and in the last two years only half the

cases in women were recognized during life. This seems to indicate that insufficient attention is given to the possibility of lung cancer in women. It is emphasized that the general hospital is more likely to receive the atypical, neglected, undiagnosed cases. Cough was the initial symptom in less than half (47.6%). Presenting complaint was fatigue in 69%, dyspnea in 26.9%, fever in 7.6%, chest pain in 15.2%, hemoptysis in 8.9% and symptoms from metastases in 17.9%. Associated chronic peripheral vascular disorders were present in 25 (17%). Five patients had cancer of other sites. Four, in the rectum, gingiva, lip and skin, had been treated with good results. One patient had untreated prostatic cancer.

Seven patients died without metastases, one of hemoptysis, one of widespread pulmonary tuberculosis and 5 of pulmonary infection directly connected with the lung tumors, 3 of these were over 70. Four had metastases only to hilar nodes and should have been operated on. Of these 11 patients who might have been benefited by surgery, 4 were over 70.

**Physiologic Aspects of Bronchogenic Carcinoma** Seymour M. Farber, Roger H. L. Wilson, David A. Wood and Orville F. Grimes<sup>6</sup> (Univ. of California) state that surgical therapy of bronchogenic carcinoma demands preoperative study of pulmonary function. Besides extension and metastasis of the tumor itself, lack of adequate pulmonary reserve is probably the only major contraindication to pneumonectomy. In patients with poor pulmonary function, respiratory crippling has occurred after a pneumonectomy.

Simple ventilation studies and inspiration expiration posteroanterior x rays are sufficient in many cases. Maximum breathing capacity, resting exercise and recovery ventilatory tests, correlated to give ventilatory coefficients and spirographic tracings are simple to perform. Fluoroscopy can detect weakness of the diaphragm. Chest x rays can be correlated with vital capacity tests. Fluoroscopic study of the heart, electrocardiograms, hematocrit values, venous pressure and circulation time are important in determining the status of the heart, especially the right side. Simultaneous intrapleural pressure readings are important.

(6) J. Thorac. & Surg. 31:245-250, February, 1956.



Many patients need more complicated studies. Determination of residual air and intrapulmonary gas mixing can be done but does not differentiate between the two lungs. Bronchspirometry is the best single differentiating function test though it is limited because of the discomfort it causes. It is the most accurate technic for determining volume ventilation, oxygen consumption and intrapulmonary mixing for each lung separately and is important in assessing the condition of a single lobe. Blood studies can be performed to determine arterial oxygen and carbon dioxide tension.

Pre-existing pulmonary abnormalities are common in patients with bronchogenic carcinoma including emphysema, fibrosis and pleural thickening. It is often difficult to isolate the effects of the tumor from general pulmonary insufficiency. Every effort must be made to determine the efficiency of the other lung.

Inadequate ventilation during surgery and in the early postoperative phase may readily occur. Ventilation during surgery usually is not a problem because it can be controlled by the anesthetist. Periodic check of the arterial carbon dioxide tension is important. When respiration is shallow after the thorax is closed but before the patient completely recovers consciousness, the intermittent positive pressure apparatus is better than the use of oxygen alone since it restores adequate ventilation, preventing accumulation of carbon dioxide as well as ensuring normal oxygen content in the alveoli. Pleural effusions, atelectasis, paradoxical respiration and pericardial tamponade may diminish respiratory efficiency postoperatively. Painful respiration, the most frequent cause of postoperative respiratory embarrassment, can be controlled with paravertebral alcohol block or procaine infiltration of the incision.

In the late postoperative phases, scoliosis is perhaps the greatest danger, especially after pneumonectomy with thoracoplasty. It can be prevented by diligent physical therapy. Palliative radiotherapy should not be used without pulmonary function tests in patients with respiratory embarrassment.

**Natural Duration of Bronchial Carcinoma** J. R. Bignall<sup>7</sup> (London) reports that of 637 patients seen during 1951 and

(7) Lancet 2:210-214, July 30, 1955.

1952, 255 were untreated. Half the 255 patients died within nine months of appearance of first symptom, and 14% survived two years or longer. Histologically, the tumor was squamous carcinoma in 73, adenocarcinoma in 11 and undifferentiated carcinoma in 45.

Median survival time of those with differentiated tumors was  $11\frac{1}{2}$  months, 46% surviving longer than 1 year and 25%, 2 years or more. Half those with undifferentiated growths were dead within  $7\frac{1}{2}$  months, and the proportions surviving for 1 and 2 years were only 31 and 7%. The difference at two years was 18%, with a standard error of 6%. Of 66 patients with symptoms for less than three months 50% died during the next five months and 26% within three months. Prognosis became worse with increasing length of history until median survival time from diagnosis was only three months in those ill for four to five months. In those ill longer than five months before diagnosis, prognosis improved. Among 32 with history of a year or longer median survival time after diagnosis was seven months, only 28% dying in the next three months and 31% living at least another year.

Total duration of illness from start of symptoms was shorter in those with metastases at diagnosis, 94 were patients having a median survival time of  $7\frac{1}{2}$  months, 27% surviving for longer than 1 year and 5% for 2 years. Median survival time was  $11\frac{1}{2}$  months for 161 patients with no clinical or radiographic evidence of metastases at diagnosis, the 1 and 2 year survival rates being 46 and 22%.

Duration of life appeared to depend, though to less extent on nature of the first symptom and age of the patient but was not materially influenced by sex or by the lobe in which the tumor occurred. Patients with illness beginning with chest pain were in a more advanced stage of the disease than those with hemoptysis or fever as first symptoms. Duration of life seemed to increase with age.

Relation of duration of life after diagnosis to length of history before diagnosis is not simple. Poorest prognosis was found in those with symptoms for four to five months before diagnosis, half of them dying in the next three years. Half those with symptoms for a year or more lived a further seven months and almost a third for another year.

**Alveolar Cell Carcinoma of Lung (Pulmonary Adenomatosis):** Study of 155 Cases, 10 Reported for First Time, is presented by H. Ryerson Decker<sup>8</sup> (Pittsburgh). Alveolar cell carcinoma does not resemble any other growth. Grossly, its two forms are (1) nodular, multiple growths distributed throughout one or both lungs and (2) a diffuse form suggestive of coalescence of the nodules. Both may occur simultaneously.

The nodules are milium to marble size, yellowish gray, whitish or pink, globular and firm, with fairly sharp borders. The diffuse form resembles pneumonia in a stage of gray hepatization involving a lobe or even an entire lung. Unilateral or bilateral pleuritis with fibrinous or serous exudate and adhesions may occur. Cavities and bronchiectasis are rare. Bronchi or bronchioles are not involved by tumor. Generally, lung changes are more extensive than physical or x-ray signs indicate. Metastases are not prominent or early. They were found in 53 of 117 (about 45%) autopsies. When present, they extend by the lymphatics or blood stream into tracheobronchial (hilar) lymph nodes, pleura, distant lymph nodes, pericardium, liver, kidneys, adrenals, brain and skeletal system.

Microscopically, the prominent feature is that the interalveolar septa are lined but not invaded by columnar cells, which show all degrees of proliferation and form papillary projections into the alveolar lumen. The cytoplasm is clear and may be pink staining. Nuclei and cells vary in size. Opinion varies as to origin of these cells.

In the 155 cases reviewed, sex incidence favored males 32. Two patients were Negroes, one a Japanese. Age range was 17-83, with a peak in the 6th decade. Family and past medical histories and occupation yielded no findings of apparent etiologic significance. Onset usually was gradual, but in 22 was ushered in by an acute respiratory attack; the disease was asymptomatic in 2. Earliest and most constant symptom was cough, which in all but nine, was productive of sputum varying from 30 to 1,500 cc in 24 hours. Dyspnea, usually progressive, was noted in 81. Weight loss and fatigue were not prominent. Cyanosis was present in 20, hemoptysis in 13 and streaking of sputum in 4. Fever, ap-

parently with definite infection of the lung, was present in 20%. After appearance of symptoms, the clinical condition deteriorated progressively, slowly or rapidly until death, except in patients relieved by surgery. Decline was hastened by intercurrent infections and development of metastases. Death was caused by asphyxia due to replacement of respiratory epithelium, heart failure or complicating pulmonary infection. Duration of illness before treatment varied from a few weeks to five or six years. In 80%, duration was less than a year. Most patients, when hospitalized, were gravely ill and died within six months.

Physical signs paralleled degree of infiltration, consolidation or pleural effusion. The blood picture changed with duration and degree of infection. In general, anemia was not a factor. Sputum examination for malignant cells gave positive results in 18 of 42 patients. The earliest lesions appeared as light, patchy infiltrations on x-rays. Later nodular lesions appeared. They were usually multicentric and often coalescent so that they formed a mass or massive pneumonic consolidation. Pleural fluid was present in 10%. X-ray appearance could not be distinguished from adenocarcinoma, metastatic carcinoma, primary tuberculosis, sarcoid granuloma, fungous disease or bacterial pneumonitis. Bronchoscopy and bronchography proved of little value except negatively in 21 patients.

Diagnosis of alveolar cell carcinoma is difficult to make during life. It is certain only if characteristic tumor cells are demonstrated in the sputum or pleural fluid obtained at biopsy or thoracotomy or by biopsy of cervical lymph nodes. It was diagnosed correctly in only 32 patients before death though carcinoma was diagnosed in 23 others.

Surgery, the only treatment that offers a chance for recovery, is probably less successful than in bronchogenic carcinoma because alveolar cell carcinoma is often multicentric and bilateral in its early stages. Of 50 patients operated on, 11 were living and well 10 years later and 4 survived over 5 years, 5 of the 11 had had pneumonectomies and 3 lobectomies. There were eight postoperative deaths.

Among the 10 patients reported on by Decker, definitive operation (pneumonectomy) was performed in only 2. One died 36 hours after operation, the other was living and well 2 years later.

► [The article abstracted here is an excellent review of the whole subject.—Ed ]

**Surgical Considerations in Pulmonary Coccidioidomycosis.** Report of 100 Cases. Bert H Cotton, George A Paulsen and J W Birsner<sup>9</sup> state that the military stationing of personnel in southern California and southwestern states and the rapid postwar expansion of the population in Los Angeles County and San Joaquin Valley have led to the increased incidence of pulmonary coccidioidomycosis. The disease can now be found anywhere in the world. Complications of acute coccidioidomycosis in the lungs are (1) extreme hilar adenopathy, (2) coccidioma, (3) pleural effusion, (4) bronchiectasis, (5) fibrosis, (6) cavitation and (7) dissemination. All the pulmonary complications, except fibrosis and dissemination, create problems of diagnosis for the thoracic surgeon.

Coccidioidal cavities are chronic and persist without a zone of fibrosis. They should be removed surgically to prevent further complications. Medical care is not adequate treatment. Indications for surgery are (1) giant cavity, (2) secondarily infected cavity, (3) check-valve cavity, (4) ruptured cavity (pleural effusion, spontaneous pneumothorax, empyema, bronchopleural fistula, nonexpansile lung), (5) coccidioma and (6) continued and severe hemoptysis. A giant cavity is one larger than 5 cm. The cause of progressive enlargement of a cavity is secondary infection. The check-valve mechanism of a cavity is due either to the membrane formed by secondary infections or to endobronchial disease, and the condition must be treated surgically to prevent cavity rupture. The commonest complication of a ruptured cavity is pleural effusion, which must be treated by aspiration. Spontaneous pneumothorax is due to rupture of a cavity having a residual large, open bronchus. Immediate surgery is necessary to close the fistula and to clean the pleural space. Empyema must be treated surgically as soon as possible. A bronchopleural fistula must be treated by an extrapleural type of decortication and wedge removal of the cavity. Nonexpansile lung is due to a pleural effusion not adequately treated and to delay in surgical treatment of a ruptured cavity.

A coccidioma is a form of focalized lesion of the pulmo-

nary infection and may be true coccidioma or pseudococcidioma, which is a small cavity filled with inspissated material. The coccidioma is granulomatous, appearing as a coin lesion. Coccidiomas must be removed when diagnosis is in doubt and a tumor is suspected, and when it enlarges or has a cavity, both due to secondary infections. Hemoptysis must be treated surgically to prevent severe hemorrhage from erosion of a large blood vessel.

The risk of disseminating disease following surgery is almost negligible after the acute phase of the disease is over. Surgery is not performed until six months or more after the acute phase of the infection. Preoperative work-up includes localization of the cavity and bronchography, because bronchiectasis often is associated with a cavity. Operations include lobectomy, segmental and wedge resections by the usual techniques. Lobectomies are performed by the individual ligature technic. After wedge resection the resected lobe is closed in the manner of a fan.

Of 100 cases, the surgery was pneumonectomy in 14, lobectomy in 41, segmental lobectomy in 35, pulmonary resection in 9 and decortication in 1. Diagnosis was confirmed in all either pre- or postoperatively by complement fixation test, sputum examination, culture, animal inoculation and/or histologic examination. There were few complications and the results were excellent. There was only one postoperative death. Further cavities developed in two patients and secondary operations were performed, one patient had a residual coccidioidal cavity and the other had a tuberculous cavity.

**Pulmonary Histoplasmosis** is reported by Thomas F. Puckett<sup>1</sup> (Fitzsimons Army Hosp., Denver) in 58 men and 9 women, nearly half of whom were aged 21-30. Histoplasmosis, a highly infectious mycosis caused by *Histoplasma capsulatum*, is endemic in the Mississippi and Ohio valleys and along the Appalachian Mountains. The usual route of infection is the respiratory passage, giving rise to a primary focus, or foci, within the lungs. Primary histoplasmosis is clinically indistinguishable from common upper respiratory infections and may be asymptomatic. It usually has a short benign course. Healing may result in complete resolution but more frequently leaves one to many discrete, scattered,

(1) Am J Surg 90:92-100, July 1955

fibrotic or, oftener, calcified lesions in one or more lobes. In a small percentage of cases the primary form is progressive, resulting in disseminated histoplasmosis, usually characterized by involvement of all organs. Disseminated histoplasmosis is usually fatal.

Chronic active pulmonary histoplasmosis closely mimics pulmonary tuberculosis, is intermediate between uncompli-



Fig. 36—Hilar node resulting in middle lobe syndrome; note compression of bronchus. (Courtesy of Puckett, T. F. *Am. J. Surg.* 90:92-100, July 1955.)

cated primary and widely disseminated histoplasmosis and is amenable to definitive surgical therapy.

In all 67 patients pulmonary tissue, hilar nodes, or both, were removed and *H. capsulatum* was identified in the resected material. All were considered to have healed or healing primary histoplasmosis. The chest condition was asymptomatic in 31. The symptoms of the others included malaise, easy fatigue, weight loss, blood-streaked sputum, frank hemoptysis, upper respiratory symptoms, fever, and

transient pleural pain. Physical examination was usually noncontributory. Preoperative cultures of sputum and gastric washings for fungi and acid-fast bacilli were negative in nearly all cases, but tissue sections stained by the periodic acid-Schiff stain were positive for *H. capsulatum* in all cases.

Reaction to the intracutaneous histoplasmin test was positive in all but one patient. In some patients, intracutaneous coccidioidin and tuberculin reactions were also positive. Re-

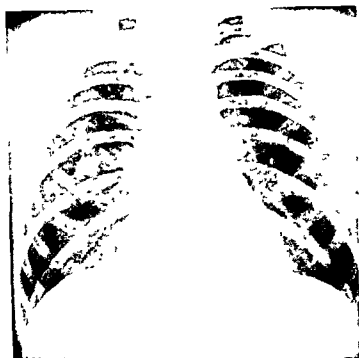


Fig. 37—Focalized histoplasmosis, typical of coin lesion seen in many cases (Courtesy of Puckett, T. F., *Am J Surg* 90:92-100, July, 1955)

sults of the complement fixation test were negative in 15 patients and positive in the others at from 1:5 to 1:64 dilution. Results of the collodion agglutination test were negative in 23 and positive in the others at from 1:1 to 1:4 dilution. In acute primary self-limiting histoplasmosis, the complement fixation antibody appears early, with a peak titer of 1:80 to 1:2560 within six weeks of onset. These titers remain for only a short time, and by the fourth month are usually 1:20 or less. In chronic histoplasmosis, the titer remains higher (1:160 or more), and clinical improvement is accompanied by gradual fall. In advanced generalized histoplasmosis, the titers are low or antibodies are not



fibrotic or, oftener, calcified lesions in one or more lobes. In a small percentage of cases the primary form is progressive, resulting in disseminated histoplasmosis, usually characterized by involvement of all organs. Disseminated histoplasmosis is usually fatal.

Chronic active pulmonary histoplasmosis closely mimics pulmonary tuberculosis, is intermediate between uncompli-



Fig. 36—Hilar node resulting in middle lobe syndrome, note compression of bronchus (Courtesy of Puckett T. F. *Am. J. Surg.* 90:92-100, July 1955.)

cated primary and widely disseminated histoplasmosis and is amenable to definitive surgical therapy.

In all 67 patients, pulmonary tissue, hilar nodes, or both, were removed and *H. capsulatum* was identified in the resected material. All were considered to have healed or healing primary histoplasmosis. The chest condition was asymptomatic in 31. The symptoms of the others included malaise, easy fatigue, weight loss, blood-streaked sputum, frank hemoptysis, upper respiratory symptoms, fever and

transient pleural pain. Physical examination was usually noncontributory. Preoperative cultures of sputum and gastric washings for fungi and acid-fast bacilli were negative in nearly all cases, but tissue sections stained by the periodic acid-Schiff stain were positive for *H. capsulatum* in all cases.

Reaction to the intracutaneous histoplasmin test was positive in all but one patient. In some patients, intracutaneous coccidioidin and tuberculin reactions were also positive. Re-



Fig. 37—Focalized histoplasmosis, typical of coin lesion seen in many cases (Courtesy of Puckett, T. F.: *Am. J. Surg.* 90, 92-100, July, 1955.)

sults of the complement fixation test were negative in 15 patients and positive in the others at from 1:5 to 1:64 dilution. Results of the collodion agglutination test were negative in 23 and positive in the others at from 1:1 to 1:4 dilution. In acute primary self-limiting histoplasmosis, the complement fixation antibody appears early, with a peak titer of 1:80 to 1:2560 within six weeks of onset. These titers remain for only a short time, and by the fourth month are usually 1:20 or less. In chronic histoplasmosis, the titer remains higher (1:160 or more), and clinical improvement is accompanied by gradual fall. In advanced generalized histoplasmosis, the titers are low or antibodies are not

demonstrable Results of serologic studies were consistent with the inactive or healing lesions found

The intralobar lesions were found in all lobes, and hilar or mediastinal nodes only were present in three patients (Fig 36) The hilar nodes that were found in many patients represent the central component of a primary complex analogous to that seen in tuberculosis and coccidioidomycosis The parenchymal lesions were 0.5-3.5 cm in diameter and were usually round, with consistency varying from stony hard to firm and rubbery Most of them were located in the immediate subpleural region, and about half were associated with a round, oval or stellate pleural plaque that was fused to the more peripheral portion of the lesion Usually the pleural plaque extended into the main mass of the lesion to form a keystone In older lesions, the cut surface had a concentric laminated appearance, with deposits of pigment at the interfaces between the laminations In younger lesions, the cut surface was homogeneous About half the cases showed single, isolated, sharply demarcated lesions that were demonstrated as coin lesions on x ray (Fig 37)

Microscopically, the large lesions had encapsulated foci of coagulative pneumonia, with discernible alveolar outlines, except in the central necrotic portion made up of amorphous material and calcification Organisms were always found in or immediately adjacent to the central areas and were probably nonviable It was not possible to culture the organisms The lymph nodes contained granular amorphous necrotic tissue and organisms

No known recurrences or postoperative spread of histoplasmosis had appeared in any patient Postoperative follow-up has been three years in 10 patients and slightly over two in 15

**When Should Bullets Lodged in the Lung Be Removed Surgically?** L. Adelberger and H. Worn<sup>2</sup> report 20 cases in which bullets or fragments of shrapnel were removed from the lung, in most instances more than five years after original injury The time interval between first symptoms and operation varied from 1 month to 12 years In 14 indication for operation was severe at times life-threatening hemorrhage In eight instances in which the interval between on-

(2) Deutsche med. Wochenschr. 81:446-450, Mar. 30, 1956

set of symptoms and operation was not over four months (two months or less in five), the foreign body could be removed by simple pneumotomy, without loss of lung tissue. Segmental resection was performed in five patients, lobectomy in six and pneumonectomy in one. Aside from one patient in whom, after lobectomy, there was insufficient elasticity of the remaining lung tissue, and a secondary plastic operation was necessary, there were no complications or sequelae, and there were no deaths.

Severe pathologic changes in the lungs were demonstrated in several in whom first symptoms appeared several years after injury (in one patient, 27 years later). In one case, two shell fragments were lodged in the same lobe, one site remained free from reaction, but the other developed serious bronchial and parenchymal changes. Gross and superficial conditions alone are not reliable criteria for appearance of later complications. The longer operation is delayed after tissue reaction to a shell fragment occurs, the more extensive the changes in bronchial mucosa and lung parenchyma. Furthermore, with delay, operation becomes more difficult and requires wider resection of the lung. The possibility that a residual shell fragment might lead to carcinoma cannot be excluded.

Every operation on the lung must have justifiable indication. Apparently sealed off foreign bodies, without reaction in surrounding tissue, should be left undisturbed, but the slightest symptoms (recurrent bronchitis or blood-tinged sputum) are indications for surgical treatment. Early operation is necessary to avoid progression to severe and extensive pulmonary lesions. The operative risk is slight and is less when operation is performed promptly after onset of symptoms.

**Tuberculous Lesions Associated with Bronchial Cancer**  
Pathologic Study of 200 specimens of bronchogenic cancer by Jacques Delarue and Jean Paillas<sup>3</sup> (Paris) revealed that 35 (27 surgical and 8 autopsy cases) were associated with tuberculosis. Tuberculous lesions involved the parenchyma in 15 (7.5% of the total cancer series), lymph nodes in 19 and a bronchus in 1.

Parenchymatous tuberculous lesions most often (81%) involved the segment of the lung tributary to the cancerous

(3) Presse med 63 1788 1792 Dec 25 1955

bronchus Contralateral lesions were present in two cases, and in one, both sites were involved Most tuberculous lesions of the parenchyma (74%) were recent and active Most of these (63%) were of cavitory type, which is difficult to distinguish from cancer Massive caseous bronchopneumonia (19%) was almost always associated with cancer of the main-stem bronchus This is a fulminating lesion which usually appears a few days before death and may follow radiotherapy Tuberculous bronchiectasis (9%) and tuberculoma (9%) are rare but easily recognizable Parenchymal tuberculosis was associated with epidermoid tumors in 67% and anaplastic lesions in 33% In the total series there were 70% epidermoid and 30% anaplastic carcinomas Old tuberculosis was encountered only in epidermoid carcinoma In cases with active tuberculosis, the proportion of anaplastic carcinomas increased to 45% Two patients with caseous pneumonia had small cell carcinoma

Tuberculous lymph nodes at the tracheobronchial bifurcation were found in 10% of the 200 cases, often in contact with or very near the tumor Some tuberculous adenopathies were situated some distance from the tumor, particularly laterotracheally Some of the lymph nodes were large, and others showed no hypertrophy Tuberculous glands showed fibrocaseous hyalin lesions in 70%, follicular in 25% and caseous in 5%

In performing pulmonary resections, surgeons aim to remove all malignant lymph nodes, and some recommend exeresis of all cellular mediastinal nodes, regardless of size In numerous cases, even large lymph nodes may be tuberculous, but there are no macroscopic signs to distinguish them from malignant adenopathies These tuberculous glands pose serious problems which can be resolved only by immediate histologic examination during operation

Although coexistence of bronchial cancer and pulmonary tuberculosis is well known it is often difficult to prove clinically Search for bronchial cancer is not necessary in all cases of tuberculosis but should be considered in patients in whom tuberculous lesions develop during the fourth and fifth decades In such instances tuberculosis is likely to be of cavitory type with radiologic appearance similar to that of bronchial cancer Repeated cytologic examination of sputum may reveal presence of bronchial tumor in some

cases of this type Tuberculous lesions were recognized before operation or autopsy in only a third of the patients with known bronchogenic cancer.

Detailed pathologic study of tuberculous lesions reveals (1) frequent localization in the parenchyma tributary to the cancerous bronchus and (2) frequency of active lesions, notably in anaplastic carcinoma It is concluded that the preponderant localization of pulmonary tuberculosis in the parenchyma tributary to the cancerous bronchus is not due to chance If tuberculosis favored development of cancer because of chronic irritation tuberculous lesions should be seen in the bronchi instead of the parenchyma Frequency of active lesions and the fact that some bronchial cancers (particularly epidermoid) develop slowly indicate that tuberculosis must develop after the tumor Others have noted that irradiation of a bronchial cancer may produce "activation" of coexisting tuberculosis Thus bronchogenic cancer represents an important general or regional cause of tuberculosis

**Biochemical Decortication by Means of Hyaluronidase in Chronic Pleural Empyema** of tuberculous origin was carried out by W Bross and T Garbinski<sup>4</sup> (Wroclaw Poland) in 36 patients, aged 19-59 who had failed to respond to conservative therapy Empyema had been present six months to five years

Treatment was carried out with a 1:50 hyaluronidase solution according to the method of Claude and Duran Reynals The titer of hyaluronidase was measured by Zablocki's method The enzyme was injected intrapleurally after previous puncture and irrigation of the cavity with physiologic salt solution Air was withdrawn with the Potain apparatus until high negative pressure was obtained Intrapleural application of hyaluronidase was begun with 2 cc solution, repeated every other day or twice a week this was usually increased to 20 cc Administration of hyaluronidase for 8-12 weeks stimulates specific antibodies in the exudate These decrease after some weeks, and administration of hyaluronidase must be controlled in individual courses by results in the exudate

Results in 24 patients were successful, with complete healing of the cavity, in two to six months In 12 who showed

(4) Schweiz med Wchnschr 85 774 777 Aug 6 1955

no re-expansion of the lung, results were classified as unsuccessful though the discharge became thin and serum-like; 6 of the 12 were later operated on. They showed shrinking even though the process was not complete. In no instance was there deterioration in the general condition or appearance of a bronchial fistula that had not been demonstrated previously.

It is concluded that hyaluronidase in conservative treatment of chronic pleural empyema facilitates resorption of exudates, causes them to flow more readily, facilitates the effect of antibiotics on the bacteria, loosens the coating covering the lungs and allows re-expansion. Intrapleural injection of hyaluronidase causes no complications and has no effect on the healthy pleural layers which lie under the layer of fibrous tissue. In shrunk lungs, irreversible narrowing of bronchi or large bronchial fistulas, hyaluronidase, has little therapeutic effect, aside from thinning the exudate. Indication for its use in pleural empyema is, in general, the same as that for mechanical decortication

---

## THE THORAX AND MEDIASTINUM

**Complete Extirpation of Thoracic Duct: Use in Management of Primary Benign Tumor Producing Spontaneous Chylothorax.** Elmer R. Maurer<sup>5</sup> (Univ. of Cincinnati) presents a case which he believes to be the first authenticated one of true benign tumor of the mediastinal thoracic duct successfully treated by excision.

Woman, 37, had pain and tightness in the right lower abdominal quadrant but no tenderness. She had no chest symptoms, but breath sounds were diminished and the percussion note was impaired over the lower right side of the chest. A chest x-ray revealed fluid in the right lower thorax. Thoracentesis yielded 1,000 cc. of creamy, tan, odorless fluid, the consistency of whole milk. The fluid was sterile and contained no neoplastic cells. The patient was treated with multiple thoracentesis and closed-tube thoracostomy drainage over three weeks, with removal of about 7.5 L. of chylous fluid, without improvement.

Exploratory thoracotomy revealed a bulge of the lower portion of the mediastinum, chyle was leaking from a small aperture in the midportion of the bulge. The mediastinal pleura was opened widely,

(5) J A M.A 161 135-138, May 12, 1956.

exposing a long, soft, elastic, cylinder-shaped tumor, 2 cm in diameter, replacing the thoracic duct in the space between the azygos vein posteriorly, and the aorta, medially. Chyle constantly leaked from several pinpoint openings in the lower portion of the tumor. The tumor involved the entire thoracic portion of the duct, from the aortic hiatus to a point near the thoracic inlet beyond the level where the duct crosses the midline into the left side of the chest. The entire thoracic duct containing the tumor was removed. She did well and was still well after two years. The final microscopic diagnosis was lymphangioma of the thoracic duct.

This case demonstrates that the main thoracic duct can be ligated with impunity and that extensive portions can be excised without endangering life.

*Eventration of the Diaphragm, according to Harold W. Neuman, F. Henry Ellis, Jr. and Howard A. Andersen,*<sup>6</sup> is a condition in which one hemidiaphragm or a portion of a hemidiaphragm lies abnormally high in the thorax. The cause is probably a congenital developmental anomaly. In most cases the hemidiaphragm is a thin translucent membrane containing few or no muscle fibers. Occasionally the diaphragm is normal. The phrenic nerve is usually normal.

Symptoms, rarely present, are referable to the respiratory, digestive or cardiovascular system. Respiratory symptoms include cough, wheezing, shortness of breath, pain in the thorax and cyanosis. Eventration in newborn infants may cause acute episodes of severe dyspnea and cyanosis, which may result in death. Symptoms referable to the digestive tract include upper abdominal discomfort or pain, fulness and belching with or without relation to meals, regurgitation and vomiting, anorexia, heartburn and pain on swallowing. Cardiovascular symptoms include palpitation, tachycardia and pain simulating coronary insufficiency.

In cases of partial eventration, abnormal physical findings are usually absent, and in most cases of total eventration physical examination yields little diagnostic information. Frequently, diminished intensity of breath sounds and diminished or absent vocal fremitus are noted over the lower pulmonary field posteriorly and laterally on the side of the lesion. Bowel sounds may be heard in the thorax. Diminution or absence of respiratory excursion of the affected hemidiaphragm may be detected.

The diagnosis is usually established by radiologic ex-



no re expansion of the lung results were classified as unsuccessful though the discharge became thin and serum like 6 of the 12 were later operated on. They showed shrinking even though the process was not complete. In no instance was there deterioration in the general condition or appearance of a bronchial fistula that had not been demonstrated previously.

It is concluded that hyaluronidase in conservative treatment of chronic pleural empyema facilitates resorption of exudates causes them to flow more readily facilitates the effect of antibiotics on the bacteria loosens the coating covering the lungs and allows re expansion. Intrapleural injection of hyaluronidase causes no complications and has no effect on the healthy pleural layers which lie under the layer of fibrous tissue. In shrunken lungs irreversible narrowing of bronchi or large bronchial fistulas hyaluronidase has little therapeutic effect aside from thinning the exudate. Indication for its use in pleural empyema is in general the same as that for mechanical decortication.

## THE THORAX AND MEDIASTINUM

**Complete Extirpation of Thoracic Duct Use in Management of Primary Benign Tumor Producing Spontaneous Chylothorax** Elmer R. Maurer<sup>5</sup> (Univ. of Cincinnati) presents a case which he believes to be the first authenticated one of true benign tumor of the mediastinal thoracic duct successfully treated by excision.

Woman 37 had pain and tightness in the right lower abdominal quadrant but no tenderness. She had no chest symptoms but breath sounds were diminished and the percussion note was impaired over the lower right side of the chest. A chest x ray revealed fluid in the right lower thorax. Thoracentesis yielded 1000 cc of creamy tan odorless fluid the consistency of whole milk. The fluid was sterile and contained no neoplastic cells. The patient was treated with multiple thoracentesis and closed tube thoracostomy drainage over three weeks with removal of about 75 L. of chylous fluid without improvement.

Exploratory thoracotomy revealed a bulge of the lower portion of the mediastinum chyle was leaking from a small aperture in the midportion of the bulge. The mediastinal pleura was opened widely

(5) JAMA 161 135 138 May 12 1956

exposing a long, soft, elastic, cylinder-shaped tumor, 2 cm in diameter, replacing the thoracic duct in the space between the azygous vein posteriorly, and the aorta, medially. Chyle constantly leaked from several pinpoint openings in the lower portion of the tumor. The tumor involved the entire thoracic portion of the duct, from the aortic hiatus to a point near the thoracic inlet beyond the level where the duct crosses the midline into the left side of the chest. The entire thoracic duct containing the tumor was removed. She did well and was still well after two years. The final microscopic diagnosis was lymphangioma of the thoracic duct.

This case demonstrates that the main thoracic duct can be ligated with impunity and that extensive portions can be excised without endangering life.

**Eventration of the Diaphragm**, according to Harold W. Neuman, F. Henry Ellis, Jr. and Howard A. Andersen,<sup>6</sup> is a condition in which one hemidiaphragm or a portion of a hemidiaphragm lies abnormally high in the thorax. The cause is probably a congenital developmental anomaly. In most cases the hemidiaphragm is a thin translucent membrane containing few or no muscle fibers. Occasionally the diaphragm is normal. The phrenic nerve is usually normal.

Symptoms, rarely present, are referable to the respiratory, digestive or cardiovascular system. Respiratory symptoms include cough, wheezing, shortness of breath, pain in the thorax and cyanosis. Eventration in newborn infants may cause acute episodes of severe dyspnea and cyanosis, which may result in death. Symptoms referable to the digestive tract include upper abdominal discomfort or pain, fulness and belching with or without relation to meals, regurgitation and vomiting, anorexia, heartburn and pain on swallowing. Cardiovascular symptoms include palpitation, tachycardia and pain simulating coronary insufficiency.

In cases of partial eventration, abnormal physical findings are usually absent, and in most cases of total eventration physical examination yields little diagnostic information. Frequently, diminished intensity of breath sounds and diminished or absent vocal fremitus are noted over the lower pulmonary field posteriorly and laterally on the side of the lesion. Bowel sounds may be heard in the thorax. Diminution or absence of respiratory excursion of the affected hemidiaphragm may be detected.

The diagnosis is usually established by radiologic ex-

animation Anteroposterior, lateral and oblique views of the thorax reveal an abnormally high position of the affected hemidiaphragm, which presents a smooth, unbroken arc with no abdominal viscera above it Occasionally pneumoperitoneum, and rarely pneumothorax, may be necessary Diagnosis is more difficult to establish in cases of partial eventration The condition must be differentiated from diaphragmatic hernia, pericardial cyst, neoplasms and cysts of the liver, intrapulmonary and extrapulmonary intrathoracic neoplasms, atelectasis of the lower lobes of the lungs and tumors of the diaphragm At times a correct diagnosis is arrived at only after surgical exploration

Eventration in newborn infants may result in death from respiratory and cardiac embarrassment Lesser degrees may interfere with expansion of the lung, thus predisposing to atelectasis and pneumonia There is an increased incidence of abnormal mesenteric attachments predisposing to volvulus of the intestine There have been reports of rupture of the thinned out portion of the diaphragm during labor and of herniation of the spleen into the eventrated portion

Prompt treatment is indicated in newborn infants who are dyspneic and cyanotic because of eventration Continuous use of oxygen with the infant in the sitting position may result in symptomatic improvement Older children and adults with mild symptoms may be treated medically, with restriction of physical activity, avoidance of heavy lifting, reduction of weight, avoidance of heavy meals and use of antispasmodics Surgical treatment, necessary if conservative treatment fails, is directed toward strengthening the hemidiaphragm and lowering it to an approximately normal position The procedure most often used is imbrication or plication of the diaphragm by suture in as many layers as necessary Other procedures include incision of the diaphragm and overlapping suture, excision of the thinned out portion followed by simple suture of the edges and repair of the defect with Nylon prosthesis Thoracic abdominal and thoracoabdominal approaches have been used the thoracic being best in adults and the abdominal best in infants

**Osteoplastic Wall Thoracoplasty after Pneumonectomies** to obliterate space and decrease danger of infection, in a

one stage procedure, is described by Viking Olov Björk<sup>7</sup> (Stockholm). The operation is particularly applicable in pneumonectomy for tuberculosis, especially extrapleural resections due to empyema. In cases in which tuberculous empyema is breaking through the chest wall, it is better to resect the whole wall with the lung at once, utilizing prolonged artificial ventilation postoperatively.

**TECHNIC.**—Face-down position is preferable for anesthesia in pneumonectomy cases. With thick-walled empyema, it is sometimes



Fig. 38

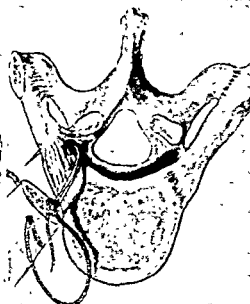


Fig. 39.

(Courtesy of Björk, V. O.: *J. Thoracic Surg.* 31:515-526, May, 1956)

preferable to do the extrapleural "strip" from the chest wall with ribs in place. Often hard work may be saved by first resecting posterior ends of upper 9 ribs on left and upper 10 ribs on right from the tip of the transverse process. After completion of pneumonectomy, rib resection is carried out as follows: Entire length of 1st rib, including costal cartilage, is resected to prevent a remaining apical air space. Ribs 2 to 9 on left and 2 to 10 on right are shortened enough to become straight, so that when they are bent or fractured in the costochondral junction, they will reach the vertebral body (Fig. 38). A drill hole is then made in the posterior end of the ribs, which are fixed to the vertebral bodies with heavy Nylon sutures through the rib holes, usually through the costovertebral ligament (Fig. 39) and behind the tip of the head of a rib. Rib 2 is fixed to the 4th, rib 3 to the 5th, rib 4 to the 6th, rib 5 to the 7th, rib 6 to the 8th and rib 7 to the 9th thoracic vertebra (Fig. 40).

(7) *J. Thoracic Surg.* 31:515-526, May, 1956.

When rib 7 or sometimes 8 has been fixed to the lowest possible thoracic vertebra, a stable wall for the mediastinum is obtained (Figs. 38 and 41). All Nylon sutures are first placed before they are tied. Intercostal nerves below the 5th intercostal space are left intact as Nylon sutures may pass between intercostal muscle bundles. The two or three lowermost resected ribs do not have to be fixed but are left outside the fixed ribs to round off the contour (Fig. 41). One drainage tube is left inside the ribs for two or three days.

With this technic, operation is usually prolonged only by



Fig 40

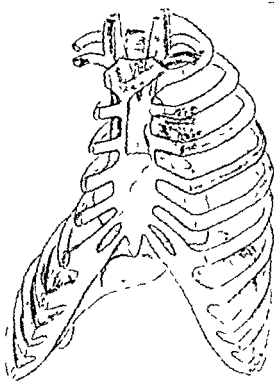


Fig 41

(Courtesy of Bjork. V O J Thoracic Surg 31 515 526, May, 1956)

about half an hour. The procedure is well tolerated even with considerable ventilatory insufficiency, provided artificial ventilation is maintained postoperatively until patients have regained strength enough for coughing and spontaneous ventilation. Of 20 patients subjected to pneumonectomy and simultaneous osteoplastic wall thoracoplasty, 3 are dead. One died after three weeks of infection with bronchial fistula, one after 10 days, with bronchopneumonia of remaining lung (autopsy showed hematoma on operated side but no source of bleeding), and the third six months after operation in cor pulmonale with pulmonary edema.

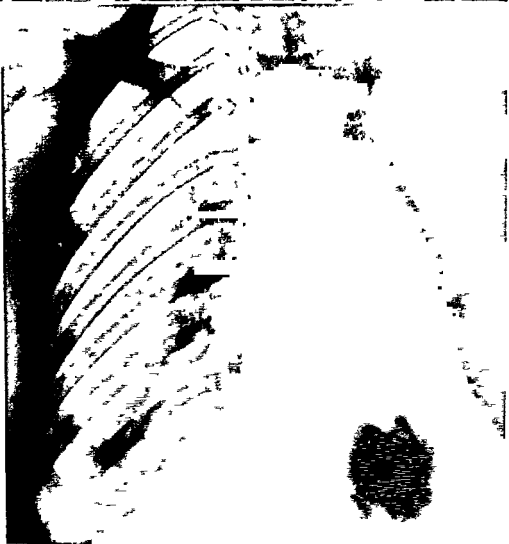
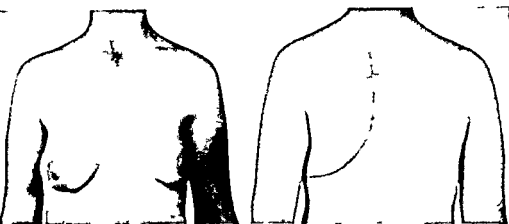


Fig 42 (top)

Fig 43 (bottom)

(Courtesy of Bjork V O J Thoracic Surg 31 515 526 May 1956)

Since prevention of infection and of herniation of the remaining lung is essential, the deformity caused by osteoplastic wall thoracoplasty has to be accepted. Figures 42, 43 show the cosmetic result in a woman, 30, after extrapleural pneumonectomy with osteoplastic wall thoracoplasty on the right side, the first rib being left in place. The patient is working full time. Maximal breathing capacity is 58 L/minute, residual capacity 24% of total. Scoliosis is slight and the mediastinum is kept in the midline.

**Mesotheliomas.** Case Reports of Primary Pleural Tumors, One Presumably Primary Pericardial Tumor and Suspicious Primary Pleural Tumors are presented by Gref and Tobriassen<sup>8</sup> (Copenhagen). In one case, diagnosed as pleural tumor or mesothelioma, autopsy showed a malignant lung tumor with invasive growth into the pleura. In another case a pedunculated giant fibroma was found, i.e., a localized giant mesothelioma with no signs of malignancy. In the remaining 10 cases, histologic examination revealed a more or less distinct mesodermal malignant tumor in the pleura. In four of these, diagnosis of malignant mesothelioma was confirmed at autopsy; there were three diffuse tumors and one circumscribed tumor. A diagnosis of presumably malignant mesothelioma was made in three patients, all died, but autopsy was performed on only one. All had diffuse tumor. In three patients, the diagnosis was judged to be mesothelioma rather than carcinoma on the basis of tissue specimens available. Two had diffuse and one a localized tumor. One patient had died, but two were still alive.

Clinical studies in these patients did not yield information of value for differential diagnosis between groups or for differentiation from carcinoma. However, all eight patients with diffuse malignant pleural tumor had more or less pronounced pleurisy with effusion as the initial sign (one with spontaneous pneumothorax), whereas two with localized tumor had no pleurisy. Fluid of increased viscosity was found in only two cases, in one with proved diffuse tumor and in one with unconfirmed localized tumor, with postoperative exudate. Five patients (representing all three groups) worked 6-30 months after operation or first hospitalization; three of them until immediately before death.

With the present histologic technic, a diagnosis of malignant

nant mesothelioma can be made with certainty only by post-mortem examination excluding primary (mainly scirrhus) carcinoma. The histologic picture is sufficiently characteristic, however, to allow a reasonably certain diagnosis. This is of practical importance in thoracic surgery, especially in the case of localized tumors. When treated by excision, the latter presumably have a better prognosis than carcinomas, and they should not be mistaken for metastases from a carcinoma.

Clinically, a circumscribed, more or less malignant pleural mesothelioma should probably be suspected when a solitary peripheral "lung tumor" is found without associated bronchial changes, while a diffuse mesothelioma should be suspected in atypical persistent pleurisy with effusion. The general condition of patients with these two types of tumor is often relatively good.

**Surgical Management of Funnel Chest** P. F. Hausmann<sup>9</sup> (Marquette Univ.) studied 51 patients with and 10 without operation. Presence, absence and degree of paradoxical motion of the lower thorax influence the decision to operate in infants. Infants do not tolerate the extensive resection of the costal cartilages necessary in the large operation, and moderate to large defects do not necessarily enlarge during the first year of life so that surgery can often be postponed until age 1. Ideal age for surgery is between the 12th and 24th month. Fixed deformity of the sternum is uncommon under age 2 but is found in older children and must be corrected surgically. Surgery should be done on every infant with marked contraction of the costal arches on inspiration.

Subperichondrial resection is necessary because (1) regeneration of cartilage or bone occurs rapidly and adequate stability of the chest wall is assured in less than two weeks and (2) by judicious placing of sutures in the perichondrium of resected ribs, the shape of the chest wall can be altered within limits so that external fixation of the sternum is scarcely necessary to insure regeneration of cartilage in the corrected position. Postoperatively physical therapy (breathing exercises), posture training and shoulder exercises are important.

In infants with small defects with little or no paradox, surgery was withheld, and in over 50% the defect disap-



## GENERAL SURGERY

peared The greater the degree of paradoxical motion, the more likely the defect was to persist or enlarge Intratracheal light plane anesthesia with generous amounts of oxygen was used The simple ligament-cutting operation was performed twice in infants not over age 4 months one having a portion of the deformed costal arches removed bilaterally The others had extensive subperichondrial resection of the costal cartilages All the deformed cartilage—sometimes the entire cartilaginous portion—of the rib was removed No recurrences or operative death, and only one minor morbidity, was noted in the 51 children, most of whom were aged 6 months to 2 years

Hypertrophy of the substernal ligament of significant degree was found in only 13 patients, thickening of sufficient magnitude to cause abnormal traction on the lower sternum being noted in 5 of these and sufficient amount of thickening to warrant the term "hypertrophy" in 8 In 38 the ligament did not thicken or change appreciably

Of the 10 patients without surgery 2 had congenital laryngeal stridor which when corrected resulted in decrease in the deformity Two with large deformities at birth had decrease in the deformity and three had small deformities that did not increase in size The others had congenital deformities and were still being observed

Hausmann believes that the deformity is primarily skeletal due to overgrowth of cartilage and not to abnormal stresses on the skeleton by hypertrophied ligaments and diaphragmatic muscles

---

 THE HEART

Surgery of Patent Ductus Arteriosus Report of Section on Cardiovascular Surgery (American College of Chest Physicians) is presented by David H Waterman (Knoxville Tenn) Paul C Samson (Oakland, Calif) and Charles P Bailey (Philadelphia) 1 Of 4 448 cases without other congenital malformations submitted by 49 collaborators 552 were eliminated due to insufficient data Among the 3 896 cases analyzed 2 929 operations were performed in children

under 14. Preoperative symptoms were absent in 69.1% of the children and 48.5% of the adults. Myocardial insufficiency was present in 27.4% of the children and 40.8% of adults. Only 3.5% of children had infection, but 10.7% of adults. Over-all surgical mortality was 2.77%—2.3% in children and 5.5% in adults. Clinical results were satisfactory in 98.3% of children and 95.5% of adults.

Division of the duct was favored by 28 (57.3%) of the surgeons, contrasted with 16 (32.7%) who preferred the ligation technic; 3 individualized on division and ligation, and 2 did not answer. Of 1,123 children operated on by ligation, 23 died (2%), whereas 34 (2.1%) deaths occurred among 1,659 children in whom the duct was divided. Mortality in adults for the two procedures was 4.3% and 5.2%, respectively.

In regard to ductal interruption in presence of pulmonary hypertension, 37 surgeons replied that it should be done, many making the reservation that no right-to-left shunt be present. Only 2 were opposed to ductal interruption, and 10 did not commit themselves. If the shunt has reversed from a predominantly left-to-right flow, only eight surgeons felt that the duct should be interrupted. All made the reservation that if pulmonary artery pressure fell after temporary clamping, the duct should be divided, but if pressure increased, the duct should not be interrupted. In presence of clearcut reversal of shunt, 31 were opposed to any interruption. All but one surgeon favored ductal interruption in absence of cardiac enlargement or clinical symptoms, though three specified that this applied to children but not to adults. Obviously, the ultimate grave dangers inherent in unoperated ductus far outweigh risk of surgery in the opinion of most cardiac surgeons.

Clinical results are predominantly good in both children and adults, but because mortality is significantly lower in children and the final result better, early operation in childhood is definitely preferable. It is generally agreed that the optimal age is 3-4 years up to 15 or 20, with 6-12 as ideal. If signs of failure appear before this, surgery should be done without delay. In patients over 40, careful individual consideration must be given. Catheterization studies are often of value, particularly if pulmonary hypertension is suspected.

## GENERAL SURGERY

► [In view of the fact that sometimes a duct that is merely ligated becomes recanalized as well as the site of a *Streptococcus viridans* infection, it is surprising to me that this statistical study has shown that actually the results of ligation on the one hand, and division, on the other, are practically the same—Ed]

**Simplified Technic for Division and Suture of Patent Ductus Arteriosus, applicable in most cases, is described by**  
**Lewis H Boshier, Jr<sup>2</sup> (Med College of Virginia)**

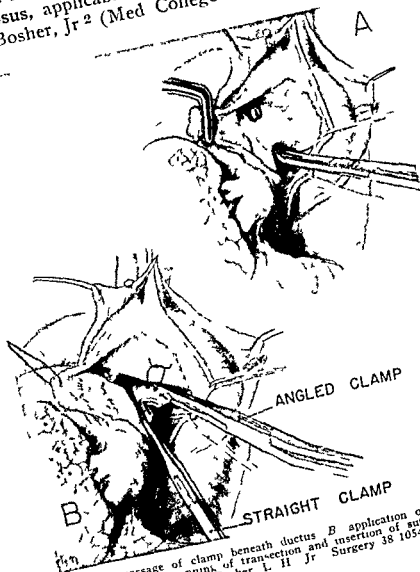


Fig 44—A passage of clamp beneath ductus B application of clamps at extreme ends of ductus technique of transection and insertion of sutures stepwise as ductus is divided (Courtesy of Boshier L. H. Jr Surgery 38 1054 1062 December 1955)

**TECHNIC**—The region of the ductus is exposed by a wide incision of the pleura through the left fourth intercostal space in the infant and child and through the bed of the fifth rib in the adult. The vagal branches of the pulmonary artery are divided. The perivascular sheath over the aorta is incised and the fibrous tissue and lappet of serous pericardium are dissected off the ductus onto the pulmonary

artery. The recurrent nerve is carefully exposed and fibrous pericardium removed from beneath the ductus. This permits passage of a clamp beneath the ductus (Fig 44 A). Angled and straight Potts ductus clamps are applied at extreme ends of the ductus (B). (The Potts bronchus clamp is now used instead of the angled ductus clamp.) Transection is started, leaving a wide aortic cuff. Interrupted

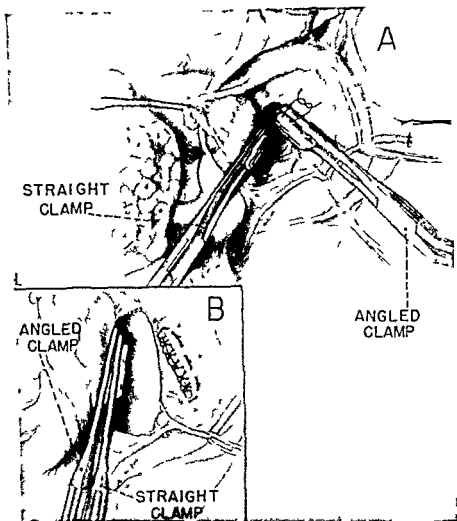


Fig 45—A completion of closure of aortic cuff B placement of angled clamp beyond straight clamp for additional length on pulmonary cuff (Courtesy of Boshier L H Jr Surgery 38 1054 1062 December 1955)

mattress sutures are inserted in stepwise fashion as the ductus is progressively divided. Complete transection of the ductus permits more adequate exposure, and closure of the aortic cuff is completed with two rows of continuous sutures or interrupted figure of eight sutures (Fig 45, A). Additional length can now be gained on the pulmonary cuff by placement of an angled clamp beyond the straight clamp (B). The pulmonary cuff is closed (Fig 46 A) and covered by serous pericardium and fibrous tissue sutured down to the fibrous pericardium beneath the pulmonary artery (B). The mediastinal pleura is sutured loosely. The pleural space is always drained by an

## GENERAL SURGERY

intercostal tube usually removed in 24-48 hours. In the adult with a large aorta and pulmonary artery and especially if the ductus is sclerotic the aortic arch above and below the ductus may be mobilized as a safeguard to permit application of a partially occluding aortic clamp.

Among 49 patients with patent ductus surgically treated

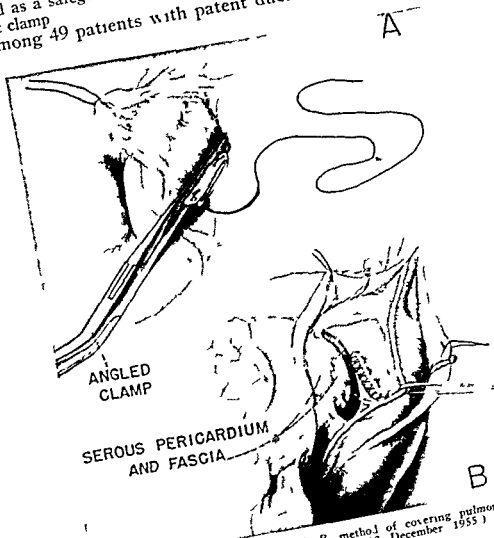


Fig. 46—A, closure of pulmonary cuff; B, method of covering pulmonary cuff (Courtesy of Boshier, L. H. Jr. Surgery 38:104, 1962; December 1955).

by the author division and suture was done in 36, 28 of the last 30 were so managed. Partial aortic occlusion clamps were utilized in seven and cross clamping of the aorta in two others in whom technical difficulties arose. One death (first case in series) occurred.

Woman 52 had auricular fibrillation, cardiac failure and tertiary syphilis. An initial attempt to ligate the ductus was abandoned because of hemorrhage and on clamping the ductus with Potts clamps the ductus snapped away cleanly from the aorta. The aorta was cross clamped but all sutures applied at the orifice promptly cut.

through under systemic pressure. The region was resected and the aorta anastomosed, but to accomplish this a clamp had to be placed proximal to the left carotid artery. Cardiac arrest resulted on final release of the aortic clamps.

No serious complications occurred in the other 48 cases. Two instances of temporary left vocal cord paralysis cleared completely, and there have been no recurrences.

**Patent Ductus Arteriosus: Postoperative Review of 51 children (40 females), with no surgical deaths, is reported by Douglas Stuckey<sup>3</sup> (Sydney).** The mothers of eight patients had had rubella early in pregnancy. In three instances, there were two affected sisters in one family. Before operation, 10 patients were short of breath on exertion, 8 tired easily and the others had no apparent symptoms. After operation, except for one child in whom recanalization occurred within a few days, all patients were active, energetic and symptom free. Before operation, many of the children were thin and underweight. In 13 for whom accurate figures were available before and after operation, the average gain during the first 12 months was 11 lb, in 10 the average increase in height was almost 4 in.

Before operation, the systolic pressure was over 120 mm Hg in 12 patients, the highest 150. Diastolic pressure was zero in three. The pulse pressure averaged 63, was less than 50 in eight and less than 40 in only three. Postoperatively, systolic pressure was over 120 in three patients, the highest reading 130. The average pulse pressure was 33, over 40 in only five, and over 50 in none. Preoperatively, a continuous murmur of classic machinery type was heard in 46, systolic and diastolic murmur in 4 and systolic murmur only in 1. In 41 there was a systolic thrill. Murmur was maximal at the pulmonary area in 33, and in 16 was more lateral in the first or second intercostal space in the midclavicular line. After operation, four patients had a continuous murmur or both systolic and diastolic murmurs. A soft systolic murmur at the pulmonary area was heard in 14, and a moderate one in 3. In 30 no murmur could be heard.

In preoperative roentgenograms the heart appeared enlarged in 27 patients. In 39 the main pulmonary artery was increased in size, and in 35 there was increased vascularity of lung fields. In 24 of 27 patients, postoperative roentgeno-

(3) M. J. Australia 1 749 751 May 21 1955

## GENERAL SURGERY

grams showed decreased heart size. The vascular markings in the lungs were less obvious in many patients, but the prominent main trunk of the pulmonary artery usually remained unchanged.

Cardiac arrest occurred in three patients during operation, all recovered after cardiac massage. In two this occurred before the ductus was ligated, and in one after the chest had been closed. Paroxysmal tachycardia occurred once, and irregular pulse was noted during operation in two others. The postoperative course was usually smooth and uneventful. One patient had persistent collapse of the lower lobe of the left lung, another had persistent left pleural effusion, which responded to treatment. In two others the postoperative course was stormy, whether due to cardiac or pulmonary factors was not determined. In both patients, persistent murmurs have suggested recurrence, probably ligation considerably reduced the ductus but still allowed a small shunt of blood from the aorta to the pulmonary artery.

**Treatment of Penetrating Wounds of the Heart.** Experimental and Clinical Observations. Denton A. Cooley, J. Ralph Dunn, H. LeRoy Brockman and Michael E. De Bakey<sup>4</sup> (Baylor Univ.) evaluate the operative and nonoperative treatment of penetrating heart wounds and pericardial tamponade in dogs and analyze penetrating wounds of the heart in 57 patients.

Pericardial tamponade was produced experimentally in dogs with saline. Aspiration of the fluid resuscitated the animals after the increased pericardial pressure caused the heart to stop. Intravenous infusions of saline enhanced cardiac filling by increasing the venous pressure despite the associated elevation of pericardial pressure. Nor-epinephrine, a vasoconstrictor, was effective in raising systolic blood pressure, even with tamponade. Alcohol decreased the tolerance to pericardial tamponade. The use of an intratracheal tube and positive pressure anesthesia was detrimental, and barbiturates reduced the tolerance for positive pressure anesthesia.

When experimental cardiac wounds were produced in dogs, about 30% died, chiefly within the first 30 minutes. Most dogs that survived the critical immediate period but died in the next few hours presumably could have been

saved by resuscitation. This suggests that patients who arrive at the hospital alive at least 30 minutes after a heart wound may have a reasonably good chance for survival. Left ventricular wounds in dogs caused a higher incidence of immediate fatality and tended to bleed more actively than comparable right-sided wounds. Lacerations to coronary vessels, particularly the anterior descending branch of the left coronary, were the most serious.

Of 57 patients with cardiac wounds, 28 were treated by nonoperative means alone, and in 14 cardiorrhaphy was attempted. About 30% died. The mortality rate of the group operated on was five times that of the nonoperative group. Although the surgical patients had the most severe injuries, there were four patients among the seven survivors of surgery in whom thoracotomy revealed that exploration was unnecessary because the laceration had sealed off completely. Complications in the nonoperative cases were not serious. In none of the patients did chronic constrictive pericarditis develop.

Nonoperative management is recommended in all cases of cardiac wounds, either as specific therapy or as a preparatory measure to emergency thoracotomy in those patients in whom response to this method of treatment is not maintained. Pericardicentesis should be performed immediately, usually parasternally through a left fifth intercostal space, and blood evacuated into a basin. If the blood is incoagulable, then it is assumed to be from the pericardial sac, but if a coagulum forms, the blood may have been withdrawn from a cardiac chamber. Pericardial aspirations may have to be repeated. Blood loss is replaced by transfusions. Glucose with nor-epinephrine should be given intravenously. Thoracotomy should be performed only if the condition becomes worse.

► [This recommendation certainly will come as a great surprise to many surgeons.—Ed.]

**Heart Wounds. Long Term Follow-up of 20 Cases** was made by James C. Drye, Walter S. Coe (Louisville, Ky.) and John P. Stamer<sup>5</sup> (Ann Arbor, Mich.). The 20 patients, studied after an interval of 3-20 years, were among 65 surviving pericardiectomy. Of 12 who are working, 7 have no symptoms and no evidence of heart disease. Of the other

(5) *Am J Surg* 91:597-599, April 1956.



five, one has arteriosclerotic heart disease and one hypertension with left ventricular enlargement and ischemia. The other three have vague chest pains and questionable dyspnea but no evidence of heart disease. Of the eight patients who are not working, four have definite heart disease, one having hypertensive cardiovascular disease with ECG evidence of an old posterior wall infarct, one an enlarged left ventricle (present before the injury), one syphilitic heart disease and one mild hypertension. No evidence of heart disease could be found in the other four nonworkers.

There were no findings attributable to the wounds and no evidence of constrictive pericarditis or false aneurysms.

**Coronary Perfusion for Longer Periods of Cardiac Occlusion under Hypothermia** Experiments reported by Norman E. Shumway, Marvin L. Ghedman and F. John Lewis<sup>1</sup> (Univ. of Minnesota) were designed to prolong the period during which intracardiac surgery could be performed; safe levels of hypothermia and to avert ventricular fibrillation by oxygenating the myocardium. That the heart extracts more oxygen from the blood than any other organ is the basis for attempted prolongation of cardiac occlusion from which animals consistently recover. By protecting the heart with oxygen brain tolerance to circulatory interruption becomes the factor determining the safe period of cardiac occlusion under hypothermia. Full advantage of the time allowed by resistance of the nervous system to hypoxia at low temperatures has not been taken previously because of failure of the heart to survive. The experiments demonstrate that perfusing the heart with blood containing venous levels of oxygen at a flow rate of 50 cc/minute permits 20 minutes of occlusion in the dog at 25°C without evidence of neurologic damage.

Ventricular fibrillation occurred in only 2 of 17 experiments. In one dog undergoing coronary perfusion with venous blood ventricular fibrillation occurred as the catheter was threaded into the aorta. Defibrillation was quickly done after which the animal withstood 20 minutes of cardiac occlusion and right ventriculotomy without relapse in to fibrillation. Consecutive long term survival was obtained in 12 dogs undergoing 20 minutes of cardiac occlusion at 25°C and right atriotomy without ventricular fibrillation.

Further clinical trial of the method was deferred after two instances in which troublesome diffuse bleeding (resulting in death of one patient) developed after surgery. Flow rate in each instance was close to 100 cc/minute. Blood was not recirculated through the oxygenator. Hearts were pink and apparently well oxygenated during perfusions. Cannulation was done through the left subclavian artery. Though both hearts fibrillated, ease of defibrillation was remarkable. Exact cause of the bleeding tendency remained obscure though the glass composition of the oxygenator may have played a part.

► [The contribution of hypothermia by Bigelow of Toronto has already demonstrated its importance, but it will probably become even more important as time goes on.—Ed.]

**Direct Vision Suture of Interatrial Septal Defect during Hypothermia** at about 26 C in 30 patients (selected from 100) was evaluated by Henry Swan, Gilbert Blount, Jr., and Robert W. Virtue<sup>7</sup> (Univ. of Colorado). Three had primum lesions, the rest were of secundum type, and five of these were associated with other cardiac anomaly. Of 27 with secundum lesions, 23 survived. One patient with a primum lesion lived, uncured. Postoperative catheterization in 21 patients showed closure of the defect in all but 2, these had massive defects which were closed by interrupted suture. After adoption of the continuous suture, there were no patients with residual shunts. Total closure of the anatomic defect is essential if the disordered function is to be corrected, 80% closure will have little or no effect on volume of the shunt.

Pulmonary pressure was within normal limits or but slightly elevated in most patients and revealed no significant changes following surgery. Patients with definite pulmonary hypertension before closure of the defect, however, revealed postoperative decrease in pulmonary artery blood pressure. Thus, with the great reduction in pulmonary artery flow and minimal changes in pulmonary artery pressure, there was a rise in pulmonary artery resistance following closure of the defect. Dyspnea and fatigue were prominent in the preoperative course in several patients, and these symptoms were greatly improved after operation. All patients returned to full activity six months after operation.

It is concluded that direct suture during hypothermia of

(7) *Surgery* 38:858-871, November 1955.

secundum type atrial septal defects is extremely effective and can be carried out at low risk. Patients with secundum defects who demonstrate a large left-to-right shunt should be offered operation at an early age, before they begin to have excessive dilatation of the pulmonary arterial tree, cardiac enlargement or progressive elevation of pulmonary resistance, since risk of operation is quite low before these changes occur. Patients with extremely high pulmonary resistance and minimal or reversed shunts have passed the stage of surgical benefit.

**Hypothermia. Part III, Clinical Application of Hypothermic Technics—Arteriovenous Cooling.** Russell Brock and D. N. Ross<sup>8</sup> report a *technic of venous cooling* that avoids interference with major arteries and permits fairly rapid body cooling. The heart is exposed before cooling, reducing the total time that the body is hypothermic. The heart can be inspected and diagnosis of any congenital anomaly confirmed at normal temperature. During cooling, any irregularities of the exposed heart are quickly detected, and resuscitative measures can be applied without delay.

Blood is sucked from a catheter in the superior vena cava inserted through the right atrial appendage, and, after being pumped through the cooling coil, is returned cold to the inferior vena cava through a catheter inserted through the same opening in the right atrial appendage. A simple hand-driven rotary pump keeps the blood circulating. The greatest safety lies in a short period of cooling followed by rapid rewarming as soon as circulatory arrest is over. The cooling is begun only after the chest is opened, and the rewarming is instituted before the chest is closed.

To have a dry heart, particularly in association with plethoric lung fields and a septal defect, it is necessary to control all veins entering the right and left atria—both the pulmonary veins and the venae cavae. Release of the venae cavae after occlusion should be slow and unsimultaneous to allow the heart to compensate for the increased load. The aorta and pulmonary artery are clamped. Clamping the aorta allows uninterrupted coronary flow, which may be the deciding factor in maintaining regular ventricular contractions.

Right ventricular cardiectomy is performed through a

<sup>8</sup> (8) Guy's Hosp. Rep. 104:99-113, 1955.

long incision over the outflow tract, sometimes extending up to the pulmonary valve ring. Atrial cardiomy is performed through a long vertical incision in the atrial wall. After the intracardiac surgery, the heart is flooded with normal saline solution and the incision clamped with a soft clamp. The edges can then be sutured. Time of exclusion of the heart from circulation in 20 patients was 6-13 minutes.

Body temperature can be conveniently recorded by the anesthetist with a pharyngeal thermometer and by the surgeon with a thermometer in the chest. In patients with septal defects, the heart and lungs may cool more rapidly than the rest of the body, including the brain.

Air embolism, control of which is not a great problem, is unlikely if the septal defect is kept uppermost and the heart is flooded with saline during closure. Coronary air embolism can be treated by puncture of a small coronary side branch and milking out of air bubbles.

Ventricular fibrillation occurring during the cooling is treated by cessation of cooling and immediate cardiac massage followed by electric defibrillation. If fibrillation occurs when temperature is low enough for safe interruption of circulation, or during cardiomy, it is disregarded and the surgery continued. Fibrillation may even help to avoid air embolism by keeping the heart quiet. Postoperatively, massage and defibrillation are performed. Intracardiac injection of epinephrine or calcium chloride or placing warm saline on the surface of the heart is useful after electric defibrillation. Prevention of fibrillation depends on maintenance of adequate coronary flow of oxygenated blood during cooling, particularly between about 36 and 28 C, and slow heart rate. Neostigmine can help in the latter. Supplementary oxygenated blood can be pumped into the system by a reversal of the circulation to maintain coronary perfusion. Differential cooling of the brain, head and arms and increased coronary flow can be achieved by cross clamping the aorta while cooling proceeds.

Rewarming should be instituted immediately after the cardiomy. Warm saline poured into the chest can be used, but venous blood stream rewarming is the most advantageous until chest closure is begun. Thereafter, surface rewarming is effective.

Deep hypothermia by means of a heart-lung machine or a differential cooling technic holds promise of longer periods of safe intracardiac surgery in the future

**Arteriovenous Aneurysm of Pulmonary Vessels** The condition consists of a shunt between one or more afferent branches of the pulmonary artery and efferent branches of the pulmonary vein. These branches are often dilated and tortuous. Larger or smaller cystic dilatations may lie between. Appearance in general is that of a vascular tumor. In 1950, Parker and Stallworth collected 78 reported cases, of these 11 were found at or verified by autopsy, 15 diagnosed clinically and 52 were operated cases, with three fatalities. Five of these patients had had bilateral operations. A relation to Rendu Osler disease was demonstrated in about 50%.

H. Eringa, R. Ter Brugge, N. G. M. Orle and L. D. Eerland<sup>9</sup> (Univ. of Groningen) report on four patients seen within six months. Mass radiography was important in detection. Two lived in the same community, and both had familial history of vascular dysplasias but nothing was known of a family relation. Two additional patients with tomographic evidence of arteriovenous aneurysm found in another mass survey had the same name as one of the two. All these patients and two brothers with marked Rendu Osler disease were traced back to the same ancestor (born in 1786). Family history in the other two patients was completely negative.

Pulmonary aneurysm apparently is a fortuitous manifestation of Rendu-Osler disease, occurring in some families and not in others. Forms with little or no hypoxia may be explained by the fact that a very large shunt is required to cause severe hypoxia. That hypoxia usually increases on exertion, short circulation time even at rest and the angiogram argue against a shunt between bronchial and pulmonary arteries though this may occur occasionally. There is no parallel between size of x-ray shadow and that of the shunt. Prognosis is doubtful and partially dependent on progression. History of the family with Rendu Osler disease with abnormalities of pulmonary vessels yielded several instances of sudden death possibly connected with the pulmonary affection.

In treatment, operation (which was successfully performed in three of the authors' patients) is advised for arteriovenous aneurysms causing subjective or objective symptoms. If affection is bilateral, indications must be individually considered. In every instance, as little functioning pulmonary tissue as possible should be sacrificed. Oximetry during surgery is important to indicate the part of the lung to be removed.

► [There is no doubt about a familial tendency in some of these cases. I operated on one of two brothers some years ago who was much more cyanotic than the other. The young man had an excellent and immediate result, but despite that the brother refused to consent to an operation — Ed.]

**Surgical Treatment for Coronary Artery Disease.** Medical Evaluation of 70 Consecutive Patients justifies its early application to most patients with coronary disease, according to B. L. Brofman<sup>1</sup> (Western Reserve Univ.). The Beck I operation, a brief, one stage procedure, provides more adequate distribution of a somewhat augmented arterial blood supply by stimulating functional intercoronary channels and extracoronary communications. Ideally, operation is performed before heart muscle is extensively damaged. Operation can prevent mechanism death and relieve areas of ischemia but it cannot restore degenerated muscle or arrest occlusive process in coronary arteries. When the heart has begun to dilate, it is too late for operation. In a patient with proved or suspected acute myocardial infarction, operation must be delayed four to six months. Advanced congestive failure precludes operation. Although rheumatic valvular disease is generally a contraindication, combined mitral commissurotomy and Beck I operation were performed successfully in seven patients. Other contraindications are intercurrent disease, such as severe hypertension with generalized vascular disease, severe diabetes, pulmonary emphysema, narcotic addiction and psychoses.

The physician must acquaint the patient with the positive approach offered by surgery, but operation should never be urged on a frightened or unwilling candidate. Generally, before operation, diagnostic procedures should be kept to a minimum, but routine studies, cardiac fluoroscopy, venous pressure and circulation time determinations should be carried out. All patients should be adequately digitalized.

(1) *Geriatrics* 10:511-515 November 1955

before surgery, even if there is no evidence of cardiac failure Digitalis decreases cardiac irritability, particularly during epicardial abrasion, decreases various supraventricular arrhythmias during induction and maintenance of anesthesia, apparently aids in maintaining normal stroke volume and heart rate during operation, definitely facilitates resuscitation of dogs—and no doubt of human beings—following cardiac arrest and patients have a much smoother operative course During operation, the surgeon, anesthesiologist and cardiologist observe close teamwork Operation is interrupted at any stage, when necessary, if alarming ECG changes appear

Although advanced age is not a specific contraindication, patients over 65 do not tolerate the operation well Among the 70 patients, ages ranged from 28 to 72, with an average of 49 Thirteen had the two stage Beck II operation After the Beck I became the procedure of choice, of the last 5 cases only 3 (55%) group III salvage patients died from coronary occlusion one to four days after operation Follow-up on the first consecutive 44 patients who survived operation (9 months to 3 years average 19 months) showed two deaths both in salvage cases, 7 months and 1 year post-operatively This long term mortality of 45% contrasts favorably with predicted mortality of 25% Sixteen patients (365%) reported no pain and 22 (50%) much less pain Full time work was possible for 27 (61%) and 10 (23%) had taken on more work since operation Four of 42 survivors had had attacks clinically suggestive of acute myocardial infarction but this was demonstrated by ECG in only one In many patients angina is decreased within a few days after operation this is followed by gradual, progressive improvement with remarkable optimism and sense of well-being No constrictive pericarditis or other deleterious effects of operation have been observed X-ray appearance is usually indistinguishable from preoperative contour Hemodynamically there is no significant change The ECG usually shows some evidence of pericarditis post-operatively, but rapidly returns to preoperative appearance Ballistocardiograms in 25 patients before immediately after and 6 18 months after operation showed improvement in 10 who previously had grossly abnormal records

**Physiologic and Pathologic Evaluation of Implantation of Internal Mammary Artery into Left Ventricular Myocardium for Treatment of Coronary Artery Disease** By quantitative retrograde coronary arterial flow, Alvin A. Bakst,<sup>1</sup> Rosario M. Mougha,<sup>2</sup> Alberto Adam and Charles P. Bailey<sup>2</sup> (Hahnemann Med. College) were able to measure and com-

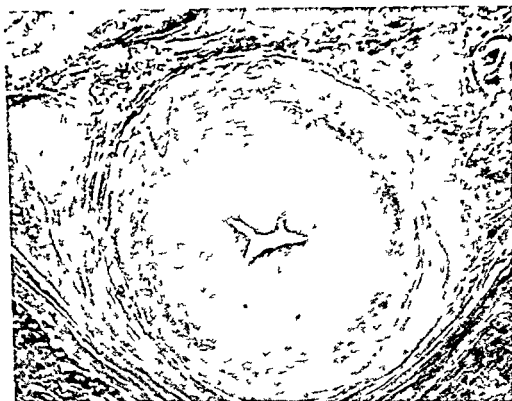


Fig. 47—Internal mammary arterial implant in the first quarter of the tunnel showing 95% reduction of lumen due to intimal hyperplasia. Collagenous cuff contains only a few small-caliber blood vessels. Hematoxylin-eosin,  $\times 26$  ( $\frac{1}{4}$  reduced). (Courtesy of Bakst, A. A. et al. *Surgery* 38:349-362, August 1955.)

pare increments of change in interarterial collateral flow in previous experiments on normal animals, those with cardiac procedures and those with arterialization of the coronary sinus. They now report experiments on a group of dogs in which the internal mammary artery was transplanted into the left ventricular myocardium.

Six months after this procedure, retrograde blood flow from the distal cut end of the ligated left anterior descending coronary artery averaged 2.3 cc/minute, representing a

(?) *Surgery* 38:349-362, August 1955.



normal amount of intercoronary arterial anastomotic flow. In all animals, the interarterial anastomotic blood flow arose almost entirely from the nonoccluded circumflex artery. These physiologic results can be explained pathologically on the basis of obliteration of the lumens of implanted vessels by intimal proliferation (Fig 47). The vessels were surrounded by fibrous tissue and appeared to be walled off by the ventricular myocardium much the same as a foreign body reaction. The presence of a few fine periadventitial vessels was believed due to terminal phases of inflammation and was not physiologically significant.

In contrast to the work of Vineberg these experiments failed to demonstrate that a systemic artery implanted into the ventricular myocardium for six months could materially increase or contribute to extracoronary collateral anastomotic flow of the interrupted left anterior descending artery.

► [These findings show it seems to me what one would expect about the work of Vineberg namely that there is not much to it. One could hardly expect that the imbedding of a long artery like the internal mammary into the myocardium would function for a long time. In fact in the illustrations accompanying Vineberg's article it is seen that the lumen of the artery is almost completely obstructed.—Ed.]

**Arterialization of Coronary Sinus for Revascularization of Heart in Coronary Artery Disease Mortality Study** Following Circumflex Coronary Artery Ligation in dogs is reported by Alvin A. Bakst, June Costas Durieux and Charles P. Bailey<sup>3</sup> (Hahnemann Med College). In normal dogs ligation of the circumflex coronary artery caused death within six hours in 90% and an eventual 100% mortality. In dogs with previous miscellaneous cardiac surgery the ligation resulted in 66% mortality. Ligation of the left anterior descending artery in dogs with previous cardiac operations resulted in 60% mortality. Two survivors demonstrated an accessory left anterior descending artery arising from the circumflex coronary artery. This probably accounted for the increase in intercoronary arterial anastomotic flow which was adequate to protect the heart against ventricular fibrillation.

In animals in which the coronary sinus was arterialized for one to two months ligation of the circumflex branch of the left coronary artery resulted in 20% mortality suggest

ing that some protection had been afforded by the preliminary procedure. In the two dogs that died within six hours, the heart had beat well for one and two hours, respectively, following the ligation, but ventricular fibrillation ensued in both within five minutes of occlusion of the vein graft. Ligation of the circumflex branch of the left coronary artery in animals in which the coronary sinus had been arterialized for six months resulted in a 66% mortality. In this group, significant protection against ventricular fibrillation by arterialization of the coronary sinus was not demonstrated. This loss of protection was accompanied by loss of retroperfusion of the myocardium, which was explained by a marked intimal proliferation and thrombosis within the major venous tributaries of the coronary sinus. In all experiments, there was no correlation between survival and coronary sinus pressure or amount of retrograde circumflex arterial blood flow.

**Coronary Artery Problem** Definition and Answer offered by Claude S. Beck<sup>4</sup> (Western Reserve Univ.) are based on about 5,000 operations on coronary vessels of dogs during 23 years and on operations on 260 patients. The problem of supplying red blood to the heart muscle in coronary disease requires uniform oxygenation of the myocardium and sufficient circulation to keep the myocardium viable so that it can continue to contract. A third of all victims of coronary disease have an unstable heart without muscle damage, 57% have an unstable heart with muscle damage and 10% have a stable heart with extensive muscle damage, and die of cardiac failure. Nothing can renew degenerated myocardium, emphasis therefore should be placed on the electrically unstable heart.

Oxygen differentials (i.e. amount of oxygen in adjacent areas of muscle which produces electric currents) must be kept below the threshold of fibrillation to maintain stability of the heart. Oxygen differentials can be reduced by uniformity of blood distribution. Autopsy study has demonstrated that intercoronary arterial channels are present in 9% of normal human hearts, such persons probably have the best chance to survive coronary artery occlusion. When occlusive disease reduced arterial diameter to 75%, incidence of intercoronaries remained at 9%. When occlusion was

complete, incidence of intercoronary arteries was 89% for acute closures and 100% for chronic closures. These findings furnish the rationale for rerouting of blood to ischemic muscle. The most effective stimulus to production of intercoronary arterial channels is reaction of inflammation from mechanical or chemical agents, and this can be incorporated into surgical operations.

The Beck I operation consists of (1) mechanical abrasion of the lining of parietal pericardium and cardiac surface, (2) application of 0.2 Gm powdered asbestos to these surfaces, (3) partial occlusion of the coronary sinus to a diameter of 3 mm and (4) grafting parietal pericardium and mediastinal fat to the heart surface. Inflammatory reaction resulting from abrasion and asbestos produces intercoronary channels. Partial occlusion of the coronary sinus provides more complete extraction of oxygen from blood, reduces oxygen differentials in the presence of coronary artery occlusion and produces intercoronary channels. Grafting tissues on the heart may bring additional blood to the heart, but effectiveness of this is often doubtful.

This operation perfuses the circumflex arterial bed with 282 cc blood/hour, available immediately after arterial occlusion. This amount of blood lowers mortality by reducing oxygen differentials and electric potentials and reduces the infarct by preserving the viability of heart muscle.

Patients chosen for operation are those with a family history of coronary disease, with coronary insufficiency or occlusion without infarct, with one or more infarcts, normal or slightly enlarged heart and ability to work. Patients with infarcts, definite cardiac enlargement and inability to work are regarded as salvage cases, some have had excellent results after operation and others have provided the mortality. Patients with infarct, cardiac enlargement and signs of failure are not acceptable. In patients with increasing angina, recent infarct or problem cases of questionable acceptability, operation is delayed until stabilization occurs or progress can be evaluated.

In the last 100 patients, mortality was 6-8%, 2 patients died of thoracotomy alone. Most had severe disease and mortality was due primarily to the disease, secondarily to operation. Present criteria for selection allow acceptance of patients with severe disease. Operation should be canceled

if blood pressure under anesthesia falls to 80 or 90 mm Hg before the incision is made

Nine of 10 patients operated on are so improved that they have little or no pain and can return to work. Most are relieved of anginal pain a few days after operation. In a few the usual signs of coronary occlusion develop after operation, this is to be expected since operation does not stop the disease process, but intercoronary circulation lessens effects of occlusion when it occurs.

Experiences with Beck Operation for Coronary Artery Disease are described by M. W. Selman<sup>5</sup> (Mount Sinai Hosp., Cleveland). The two common causes of death from this disease are ventricular fibrillation, which is sudden, and myocardial failure or muscle death, which is slow. There is experimental evidence that the Beck I operation protects the heart against death from ventricular fibrillation and prevents ischemic areas responsible for angina. This operation has significantly reduced the number and size of myocardial infarcts from coronary occlusion in dogs. Although it cannot stop the degenerative and occlusive disease in the coronary arteries or restore degenerated myocardium, it results in an increase in intercoronary and extracoronary communications, thereby augmenting the natural tendency of the heart to increase blood supply to the myocardium after coronary occlusion or narrowing.

The operation consists in partial ligation of the coronary sinus, abrasion of the epicardium and pericardium, application of asbestos powder over the surface of the heart and approximation of a pedicle or mediastinal fat to the heart. Ligation of the coronary sinus stimulates a rapid increase in interarterial coronary anastomoses. The abrasion and the application of asbestos powder to the myocardium result in development of chronic granuloma and increase in intercoronary and extracoronary communications. Approximation of vascular tissues to the myocardium provides a variable degree of extracoronary arterial blood to the myocardium.

The operation is indicated when the diagnosis of coronary artery disease has been established. Patients selected for surgery are divided into three groups, (1) prophylactic, with only mild angina or small infarct without angina, (2)

therapeutic, with moderate to severe angina, infarct followed by angina or repeated bouts of severe pain with or without ECG changes, and (3) salvage, with massive infarct or status anginosus. Most patients fall into the therapeutic group. The operation is contraindicated when there is extensive degeneration of heart muscle. Absolute contraindications include recent infarct (within four to six months), significant left ventricular enlargement, evidence of congestive failure and marked hypertension.

Preoperative measures include mild sedation, reassurance and complete digitalization. Pentothal® can be used for induction anesthesia and followed with ether, nitrous oxide or cyclopropane. Adequate ventilation is necessary. Hypotension during surgery must be corrected immediately. Blood and fluids should be replaced if lost. The ECG behavior of the heart must be followed closely during surgery with a cardioscope and arrhythmias treated. Bradycardia often occurs when the chest is opened, it can be corrected with atropine sulfate intravenously. Sinus tachycardia occurs when the pericardium is opened and usually decreases when the operation is stopped for a few minutes and the lung inflated. Rest periods during surgery prevent serious tachycardias and arrhythmias. Ventricular fibrillation must be treated with procaine, massage and a defibrillator. Cardiac standstill is treated with cardiac massage and ventilation of the lung with 100% oxygen.

An evaluation of 32 patients six months or more after they had had the Beck operation revealed that 31.3% had excellent results (able to perform full time work with little or no pain), 37.5% had good results (could do full or part time work with significant reduction in pain), 18.7% had fair results (able to perform more work than before operation with some diminution of pain) and 12.5% were unimproved.

► [It seems strange to me that this simple operation has not been employed more frequently.—Ed.]

**De-Epicardialization** Simple, Effective Surgical Treatment for Angina Pectoris is recommended as worthy of further trial by Dwight F. Harken, Harrison Black, James F. Dickson, III, and Hugh C. Wilson, III<sup>6</sup> (Boston). Preliminary experiments showed that removal of the epicardium

of the dog's heart with 95% phenol permits anastomoses between pericardial vessels and coronary arteries large enough to carry the Schlesinger mass ( $40\mu$  or larger). Subsequently, the following procedure was done on 18 patients.

**TECHNIC**—With the patient supine, optimal ventilation is assured. An incision is made in the fourth intercostal space (Fig 48). The pericardium is opened anterior and posterior to the phrenic nerve. Phenol is swabbed on the epicardium, the coronary vessels being

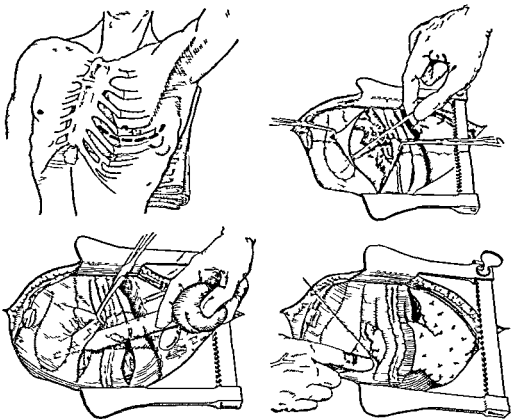


Fig 48 (top left) —Location of incision  
Fig 49 (top right) —Application of phenol to epicardium

Fig 50 (bottom left) —Talc insufflation

Fig 51 (bottom right) —Suture of lingula

(Courtesy of Harken D E *et al* *Circulation* 12:955-962 December 1955)

avoided (Fig 49). Powdered talc is then insufflated into the pericardial sac (Fig 50). The lingula of the lung is sutured in place beneath the pericardium as a source of new blood supply, and the pericardium is left open for drainage (Fig 51).

The first phenol de-epicardialization and pneumonopexy was done for severe angina present for two years after myocardial infarction.

Man 34, had dramatic and immediate relief from operation with almost complete disappearance of pain within two weeks. During the next six months with the patient on restricted activity, occasional chest pain was readily controlled by 2 or 3 nitroglycerin tab-

lets a week. In less than a year, pain disappeared. Four years later the patient was well except for occasional intermittent claudication due to extensive calcification of leg arteries which was present before operation. For 2 years he has worked full time.

All but 4 of the 17 other patients had complete relief from pain. Two had a recurrence about two months after operation, but pain was subsiding in one. Two others have psychiatric problems that make evaluation of real anginal residuum difficult. There were no operative deaths but two patients died within two months after operation of fresh coronary occlusion, though pain had been completely relieved. For this reason they were excessively active, probably before adequate collateral channels could have developed. More than half the patients had suffered previous myocardial infarction.

At present, this procedure is not being proposed for treatment of coronary insufficiency when angina is not present but is offered for relief from this distressing symptom, if it does not respond to medical treatment. There is reason to conclude, however, that a substantial improvement in coronary blood supply may also result.

► [Only time will tell whether or not this procedure will produce better results than the Beck I operation—Ed.]

**Hemodynamics of Left Side of Heart as Studied by Simultaneous Left Atrial, Left Ventricular and Aortic Pressures; Particular Reference to Mitral Stenosis.** Eugene Braunwald, Howard L. Moscovitz, Salomao S. Amram, Richard P. Lasser, Samuel O. Sapin, Aaron Himmelstein, Mark M. Ravitch and Alvin J. Gordon<sup>7</sup> (Mount Sinai Hosp. New York) studied the hemodynamics of the left side of the heart in six patients without, and eight with mitral stenosis, by simultaneous needle puncture of the left atrium, left ventricle and aorta through the open chest. Pressures were recorded simultaneously on identical base lines at identical sensitivities.

In patients without mitral stenosis, left ventricular mean diastolic pressure was 3-10 mm Hg. Mean left atrioventricular filling pressure gradient measured between 0 and 1 mm Hg. In presence of a normal mitral valve, the crossing of the left atrial and left ventricular curves, onset of the atrial c wave and presumably the moment of mitral valve closure all occur immediately after onset of ventricular contraction.

(7) *Circulation* 12:69-81, July 1955.

In mitral stenosis, crossing of the left atrial and left ventricular curves and onset of the atrial c wave are delayed until the left ventricular pressure rises to that of the left atrial. Therefore, left ventricular isometric contraction consists of two phases (1) beginning with ventricular contraction and lasting until cross-over of the left atrial and left ventricular pressure curves, (2) beginning with crossing of left atrial and left ventricular curves and ending at moment of aortic valve opening.

When the mitral valve opens, other differences between the normal heart and that with mitral stenosis emerge. In the former, the left atrial and left ventricular pressure curves virtually coincide. In the latter, the left atrial and left ventricular pressures diverge, the left ventricular pressure continues to fall while the left atrial remains elevated, producing a distinct and easily measurable pressure gradient, which is the fundamental hemodynamic expression of mitral stenosis. It results in slight shortening of the isometric relaxation phase and permits earlier onset of mitral valvular opening and of ventricular filling. Thus, time available for blood to flow into the left ventricle is increased by small increments at either end of the ventricular filling period. In patients with mitral stenosis diastasis is absent. All left atrial pressure curves before valvotomy showed continuous decline in pressure during diastole until atrial contraction.

Abolition of the elevated left atrioventricular filling pressure gradient constitutes the chief object of mitral surgery. Preoperative gradients, of 4-20 mm Hg fell significantly following valvotomy in every instance, being almost entirely abolished in three patients. Following surgical correction of the stenotic mitral valve, turbulent flow may be converted to laminar flow, the pressure gradient would then vary with flow in a simple linear fashion. The left atrioventricular filling gradient is a function of both the left atrial and left ventricular diastolic pressures. Following mitral valvotomy, significant elevations in the left ventricular diastolic pressures were noted in several patients, possibly a temporary effect on the left ventricle before adjustment to the altered dynamics. At any rate, the magnitude of the left atrial pressure, both before and after surgery, does not clearly reflect the magnitude of the left atrioventricular pressure gradient.



**Reduced Intrathoracic Circulation as Aid in Angiocardiography** Experimental Study in dogs by I Boerema and J R Blickman<sup>8</sup> (Amsterdam) demonstrated numerous advantages in delineation of vascular structures, of blocking the blood stream for 30 60 seconds Increasing intrabronchial pressure to 60 cm water greatly decreased left ventricular output Pressure recordings and roentgenologic evidence indicated that cor pulmonale need not be feared, venous return to the right heart is primarily greatly reduced In the authors' method, blood flow is impeded by elevation of intrabronchial air tension only once and for no more than 30 60 seconds Danger of raising aortic pressure too high during injection of contrast medium is eliminated when intrapulmonary air pressure is raised to 60 cm water

The method described does not require quick working film changers, thus making angiocardiography possible without expensive apparatus Filling of aortic arch and bulb and coronary arteries is readily performed, with good visibility Reduced movements of heart and vessels produce much clearer contours Diameter of the aorta is reduced to about two-thirds its normal size The left ventricle gives a clear image when filled Aortic valves can be clearly identified Filling of the coronary arteries is easily performed even from the aortic arch The time factor is of little interest, since the contrast medium remained unchanged for at least four seconds

With the catheter placed in the right auricle or right ventricle excellent visualization of the right heart, outflow tract and pulmonary arteries was obtained Visibility was maintained in the lungs during elevation of intratracheal pressure up to five seconds with a preceding injection time of equal duration In some instances, both pulmonary arteries and veins were visualized simultaneously with a contrast dose of 25 cc of 45% concentration Use of this method for aortography of the abdominal aorta has not yet been studied extensively The possibility of obtaining peripheral arteriograms by injection of a small dose of contrast medium of low concentration seems attractive Sharper contours should simplify diagnostic possibilities of vascular lesions Serial exposures of dubious lesions are possible as the contrast medium remains visible for prolonged periods

(8) J Thoracic Surg 30 179 142 August 1955

This roentgenologic study of contrast fluid in the heart and great vessels confirms Weber's view that elevation of intratracheal pressure caused a slowing down of the blood stream through the heart by compression of the right heart and the venae cavae. Clinical application of the method will be described in detail later.

**Cardiac Arrest: Study of 30 Year Period of Operating Room Deaths at Massachusetts General Hospital, 1925-54** is presented by Bernard D. Briggs, David B. Sheldon and Henry K. Beecher.<sup>9</sup> The total incidence of operating room deaths for the period (covering 189,815 anesthetic and surgical procedures) was 1,1091 and of cardiac arrests (including cases of recovery or delayed deaths) 1,1406. Cardiac arrest is the sudden cessation of demonstrable cardiac activity unexplained by gross hemorrhage, shock or asphyxia. The probable causes of operating room deaths for 1925-34, 1935-44 and 1945-54 were, respectively, cardiac arrest in 25, 10 and 50 instances, hypoxia in 10, 14 and 9, hemorrhage in 5, 4 and 14, shock in 0, 2 and 5, and moribundity in 12, 8 and 6. The incidence of fatal cardiac arrests for the three decades was, respectively, 1,1518, 1,4810 and 1,1647. In 1945-54, cardiac arrest was the probable cause of 50 of 84 operating room deaths that occurred during 103,777 surgical procedures. Cardiac arrest is thus the major cause of operating room deaths, and there has been an absolute increase in the incidence of this emergency in recent years. This increase is due to the current awareness of the problem, leading to an increased frequency of diagnosis, and the increased number of surgical procedures carried out on elderly and decrepit patients.

Cardiac arrest is 20 times more common in elderly patients, 30 times more common in poor risk patients and 5 times more common in patients with heart disease than in others. Additional contributory factors are deepening anesthesia, hypoxia, reflex phenomena and improper choice or management of anesthesia.

Emergency thoracotomy and manual systole were carried out in 58 cases of cardiac arrest with 26 recoveries. During the last 10 years the recovery rate was 37%, and during the last 5 years, 50%. Neurologic complications are infrequent

(9) JAMA 160 1439-1444 Apr 28 1956

in survivors if thoracotomy is performed within four minutes or less

**Experience with Primary Cardiac Arrest**, reported by H Bergmann, H Hartl and F Walker<sup>1</sup> (Linz), consisted of 11 instances, seen during five years, among 13,500 surgical cases. Ten occurred in the operating room. In five, lasting recovery without cerebral damage was obtained, the other six died, although in two the heart beat was restored.

Outcome of therapy in cardiac arrest depends on the mechanical component (cardiac massage) and on oxygen supply. If heart massage alone does not restore normal rhythm this can be obtained by an electric defibrillator. The effect is enhanced if all insufficient myocardial contractions are suddenly stopped and asystole established, from which normal rhythm can be reinstated. Strict adherence to certain physical factors is essential. A current of too low tension (under 55 volts) will not cause defibrillation, and too long application of current or too little contact surface between electrode and heart muscle may cause burning.

The authors describe development of a simple apparatus that fulfils all necessary conditions. Rotatory input and amperemeter provide a current of 0.5-5 amp, a second rotatory input with a voltmeter produces current between 90 and 135 volts. Outflow of electric impulse occurs through a head contact; a control lamp registers work of the transformers. The apparatus is safe, insulated against moisture, sturdy and easy to handle. Electrodes are disk-shaped and sterilizable; handles are insulated with rubber and rustproof. Space is provided for defibrillator, electrodes, ampules and syringes, laryngoscope and tubes, and necessary surgical instruments on the frame, so that these are readily available.

If repeated shock is not successful in correcting ventricular fibrillation, intracutaneous injection of 1% procaine or potassium chloride may be effective in inhibiting irritability of the myocardium and conduction system, so further applications of current may be successful.

Animal experiments and clinical results with exterior electric shock, in which electrodes are applied to the thoracic wall, have been described. The artificial pacemaker also has demonstrated its value.

**Elective Cardiac Arrest** D G Melrose, B Dreyer, H H Bentall and J. B E Baker<sup>2</sup> (London) anesthetized 33 dogs, and while the vital centers were protected by perfusion with a heart-lung machine or by reduction of the body temperature, cardiac arrest was induced by injecting 25-100 mg/ml potassium citrate into the root of the aorta. Blood was excluded from the heart by ligating the venous inflow tracts and also the pulmonary artery and aorta, so that the potassium citrate entered the coronary vessels. Arrest of the heart in diastole followed within five seconds after injection. The heart became flaccid and easy to handle, and air was easily eliminated when the heart was sutured after a token operation within the left atrium or ventricle. The heart remained pink, and serial oxygen determinations from the coronary sinus revealed that negligible amounts of oxygen were being used. After cardiac arrest for 15 minutes, blood was allowed to enter the heart, and then cardiac massage with injection of calcium chloride and occasionally epinephrine and neostigmine, produced ventricular fibrillation. Electric defibrillation was successful in only 70% of animals, and the restoration of normal activity was not reliable.

Coronary perfusion experiments in isolated hearts of rabbits, a guinea pig, a kitten and a puppy revealed that injection of 10-40 mg potassium citrate in 0.2-0.4 ml close to the hearts with coronary flows of 10-20 ml/minute stopped the heart. The least amount that would stop the heart was 1 mg/ml, no upper limit of safety was determined. Diastolic cardiac arrest occurred within 10-20 seconds of injection and could be maintained as long as the injection continued. Spontaneous beating usually started again within 90 seconds of perfusion with pure Locke's solution, but with the highest concentration of potassium citrate the interval doubled. The heart rate was normal in under a minute, and force was almost fully recovered by a further two to three minutes. One heart was arrested for 55 minutes and recovered. No hearts fibrillated as a result of the potassium citrate combined with coronary arrest and none failed to resume normal beating after perfusion with pure Locke's solution.

In intact dogs, 2 ml of a 25% solution of potassium citrate, diluted to 20 cc with blood was injected in the occluded ascending aorta, and after 15 minutes of cardiac arrest, oxygenated blood was driven through the coronary arteries from the heart-lung machine by release of the aorta clamp. Strong and regular heart contractions were resumed. In an animal protected by a reduction of the body temperature to 25 C, coronary perfusion was achieved by connecting the catheter in the aorta to a bottle containing fresh oxygenated blood under pressure, without release of the aortic clamp. A single electric shock restored normal rhythm.

**Elective Cardiac Arrest by Melrose Technic** Potassium Asystole for Experimental Cardiac Surgery Willem J Kolff, Donald B Effler, Laurence K Groves, Gerrit Peereboom, Shigeto Aoyama and F Mason Sones, Jr,<sup>3</sup> state that intracardiac operations would be more easily performed if the heart could be arrested and restarted at will and if the coronary blood flow could be stopped without damage to the myocardium during the period of arrest. Visualization would be excellent in the quiescent and dry heart. Suturing would be much simpler and air embolism could not occur. Using dogs, and closely following the technic of Melrose and associates, the authors found that elective cardiac arrest can be accomplished with potassium citrate when used in conjunction with the artificial heart lung apparatus.

The dogs were connected to the heart-lung apparatus, the aorta was clamped and potassium citrate was injected into the root of the aorta. The injection mixture consisted of 2 ml of 25% potassium citrate in 18 ml blood of which 4 to 20 ml was required to induce cardiac arrest. The average interval before the heart started beating after removal of the aortic clamp was 37 seconds. Ventricular fibrillation occurred in 1 of 10 dogs, but repetition of the procedure (potassium arrest and flushing of the coronary circulation) established normal rhythm. In some experiments, the heart distended after release of the aortic clamp, because of residual potassium effect, anoxia or the extensive myocardial wound. The distention disappeared within 3 to 15 minutes, especially when the animal's circulation was supported by the artificial heart lung apparatus.

The procedure does not cause any appreciable change in serum potassium.

Direct Vision Intracardiac Surgery by Means of Reservoir of "Arterialized Venous" Blood: Description of Simple Method and Report of First Clinical Case are presented by

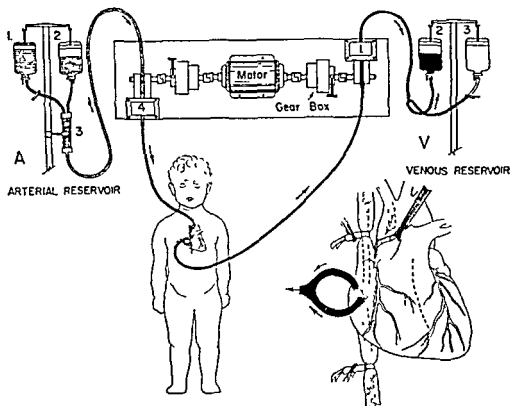


Fig 52—Arterial reservoir perfusion. A, arterial reservoir with bottles of arterial blood (1 and 2), blood filter (3) and arterial pump (4), V, venous portion of perfusion circuit with venous pump (1) and empty bottles (2 and 3) for collection of venous blood withdrawn from caval system of patient; top center, pumping assembly consisting of separate pumps at each end, driven by single motor and separate speed changers, interposed between motor and each pump head, center, relation of patient to system, lower right, close up of cannulations around heart, arterial catheter with tip just within ascending aorta and venous catheters with respective occluding tapes in proper positions in venae cavae. Rumel tourniquet around base of aorta insures dry intracardiac field by intermittent occlusion of this region if aortic valves are incompetent when heart is opened, this also selectively controls flow in coronary arterial system (Courtesy of Warden, H. E., et al. J Thoracic Surg 30 649 657, December, 1955)

Herbert E. Warden, Raymond C. Read, Richard A. DeWall, Joseph B. Aust, Morley Cohen, Newell R. Ziegler, Richard L. Varco and C. Walton Lillehei<sup>4</sup> (Univ. of Minnesota). A simple pump simultaneously delivers blood from an arterial reservoir to the arterial system of the patient and withdraws an equal volume of venous blood from the vena caval sys-

(4) J Thoracic Surg 30 649 657, December, 1955

tem Blood possessing arterial chemical characteristics is obtained from a vein of an extremity that has been exposed to external heat of 45-47 C for 15-20 minutes By preheating the arms of blood bank donors, relatively large quantities of arterialized venous blood can be collected easily

Boy, aged 6 months, weighing 4.8 kg, had a high interventricular septal defect, about 1 cm in diameter, closed under direct vision by multiple interrupted suture technic During the 14 minutes and 45 seconds of total cardiac by-pass necessary, he was perfused at a rate of 150 cc/minute (31 cc/kg/minute) by the reservoir method (Fig 52) Arterialized venous blood for the arterial reservoir was drawn a few hours preoperatively in the blood bank from eight compatible donors, the arms of whom had been heated to 45 C for 15 minutes, 3,950 cc was drawn and available for perfusion, but only 2,225 cc was needed Postoperatively, platelet count was 189,000 with normal bleeding and clotting times and hemoglobin value of 13.4 Gm Loss from chest catheters yielded only 110 cc sero sanguineous fluid during the first 48 hours Convalescence was smooth and uneventful

Seven months after operation, he had gained 7 lb 10 oz was active without limitation, had been free from intercurrent illness and was developing normally, in marked contrast to preoperative status No thrills or murmurs were present, and chest x ray showed regression of pulmonary vascular pattern to normal limits

Subsequently, this method of reservoir perfusion for total by-pass of heart and lungs for as long as 45 minutes was used successfully in five patients with various intracardiac defects

**Direct Vision Intracardiac Correction of Congenital Anomalies by Controlled Cross Circulation: Results in 32 Patients with Ventricular Septal Defects, Tetralogy of Fallot and Atrioventricularis Communis Defects** C Walton Lillehei, Morley Cohen, Herbert E Warden and Richard L Varco<sup>5</sup> (Univ of Minnesota) report a method which has been modified in four ways (1) cannulation of patient's caval system through two stab wounds in the right atrium, (2) use of a venous reservoir to prevent elevated negative pressure in afferent venous circuit, (3) alterations in pump assembly and (4) routine use of a tourniquet about the base of the aorta to provide a bloodless operating field

The root of the ascending aorta is dissected free from adjacent pulmonary artery and encircled with a cotton tape to which is attached a Rumel tourniquet (Fig 53) If the cardiotomy field is bloody, the tourniquet is occluded briefly,

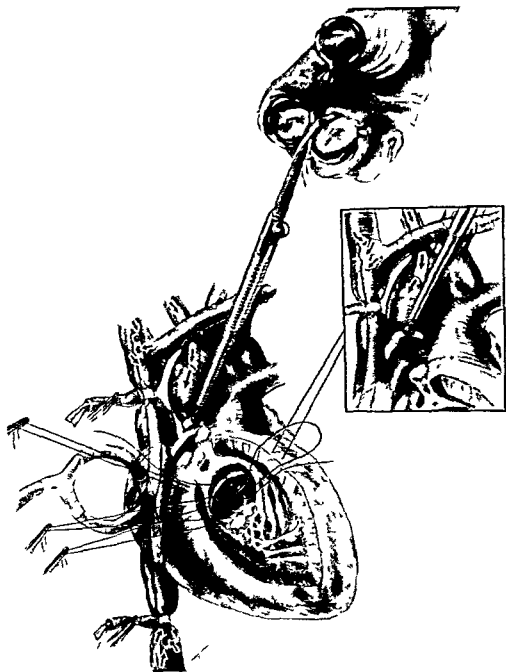


Fig 53—Aortic tourniquet permitting bloodless intracardiac operating field. Aorta is encircled as shown in all procedures in which the heart is to be opened. Note position of tape temporarily occluding ascending aorta between arterial inflow catheter in right subclavian artery and aortic valves and coronary artery orifices. Inset shows Rumel tourniquet released during phases of intracardiac procedure in which an absolutely bloodless field is not needed. (Courtesy of Lillehei C W *et al* Surgery 38 11 29 July 1955)

while inspection is carried out, and released momentarily to permit free coronary flow, and then periodically tightened and opened as required during actual suturing. This reduces blood loss via coronary flow and time needed for reparative surgery.



All 32 operations involved total cardiac by-pass for periods to 40 minutes at normal body temperatures with perfusion of patient's body at reduced rates of flow based on azygous flow experiments. No patient (or donor) had abnormal postoperative bleeding even though both were heparinized. Donor circulation takes over homeostasis promptly and automatically. The heart maintains a regular rhythm without conduction system disturbances because the myocardium is normothermic, is relieved of its pumping burden and is nourished by its coronary artery flow of blood perfectly adjusted as to oxygen, pH and electrolytes.

Among 22 children operated on for severe ventricular septal defects, the outcome was successful in 15. Six of seven postoperative deaths (all in infants under 2) were due to surgical errors (usually imperfect closure of defect) or respiratory complications. One infant, 3 months, developed complete heart block during suture, which by ECG had disappeared one hour afterward, but died 12 hours later, possibly from recurrent heart block. Defibrillation was successful in the one patient in whom ventricular fibrillation developed during closure.

Three deaths occurred among six patients operated on for tetralogy of Fallot, one due to failure to close the ventricular defect completely and one to surgical trauma to the aortic cusps. In the third, previous intrapericardial exploration for valvular stenosis left obscuring adhesions so that right ventricular cardiectomy was misplaced, resulting in cutting of the right coronary artery despite an attempt to dissect out the main coronary branches before cardiectomy. Results in three remaining cases of tetralogy of Fallot were excellent.

The outcome was successful in a gravely ill girl aged 17 months with an atrioventricularis communis defect. Pulmonary artery pressure of 90/50 was reduced after operation to 20/4 mm Hg. Death in another case of this anomaly was due to improper surgical approach through the right ventricle because of incorrect diagnosis.

The only death known to be due to heart block was in an infant, 11 months with pulmonary stenosis, a large interatrial septal defect and anomalous drainage of pulmonary veins into the right atrium and superior vena cava. All these lesions were successfully repaired but complete heart block

developed at operation and persisted until death 18 hours later

There was no donor mortality, but profound hypotension necessitating thoracotomy with cardiac massage occurred in a mother, who recovered without sequelae in 10 days. This complication arose from severe disproportion in reciprocal exchange of blood and has been obviated in later cases by the routine use of a venous reservoir between patient and pump in the venous circuit. Transfusion reaction was completely absent in all patients and donors.

**Results of Direct Vision Closure of Ventricular Septal Defects in Eight Patients by Means of Controlled Cross-Circulation** are described by C. Walton Lillehei, Morley Cohen, Herbert E. Warden, Newell R. Ziegler and Richard L. Varco<sup>6</sup> (Univ. of Minnesota). The technic for total bypass of heart and lungs consists in simultaneous reciprocal exchange of equal quantities of compatible blood from the arterial system of the donor to the patient's arterial circulation, and from the caval system of the patient to the veins of the donor. Essential functions of donor circulation are to oxygenate and revitalize venous blood received from the patient. A pump is essential to control accurately this continuous interchange of blood.

Eight patients, all seriously ill with ventricular septal defects, cardiomegaly and pulmonary hypertension, had their circulatory systems linked with suitable donors, the heart and lungs were totally by-passed for 52 1/2 minutes while the body was perfused at reduced rates of flow based on azygos flow experimental studies. Right ventricular cardiomyotomy was done with direct vision suture closure of the ventricular septal defects. All operations were carried out at normal body temperatures to obviate the deleterious effects of reduced temperature on the cardiac conduction system.

There were two deaths in infants, occurring during the convalescent period (4 and 11 days postoperatively) from respiratory complications. No patient mortality was attributable to the cross circulation method of total cardiac bypass, per se. Conduction system disturbances such as ventricular fibrillation or persistent complete heart block did not occur even though all defects were closed by direct su-

tures placed in the ventricular septum, with no effort to avoid the so called vulnerable areas. This verifies for man experimental observations indicating that the heart, euthermic and totally by-passed to reduce its work load, needs only a very reduced coronary arterial flow to remain well oxygenated, and that such a heart becomes quite resistant to induction of arrhythmias. Complete absence of air embolism, excessive hemolysis or postoperative hemorrhage was gratifying.

Four of the first six surviving patients were recatheterized four to nine months after operation, and in all four the septal defect had been completely corrected, with no remaining shunt. In two, pulmonary pressures had returned to normal. One of these patients, before operation, had noticeably inhibited body growth and severe pulmonary hypertension with apparent pulmonary arteriolar narrowing caused by multiple ventricular defects. The other two patients had pulmonary pressures still elevated above normal but less than preoperative levels. These four patients represent the first to have successful complete correction of ventricular septal defects, evidenced by disappearance of murmurs, thrills and objective postoperative catheterization studies demonstrating absence of shunt. There were no deaths or significant complications among the eight donors.

**Surgical Closure of Interatrial Septal Defects by Circumcision** is reported by Tyge S ndergaard, Henning G tzsche, Poul Ottosen and Jeppe Schultz<sup>7</sup> (Univ. of Aarhus).

**TECHNIC**—The right chest is entered through the bed of the sixth rib, and the pericardial cavity is opened 1 cm. in front of the phrenic nerve. The edges of the opening are sutured to the chest wall care being taken to liberate the caval veins sufficiently to insure unhindered flow to the heart. The two veins are encircled by a heavy silk used for traction to facilitate dissection. The cleavage between the right and left atrium is dissected as far down as possible. Usually a small vessel must be severed just in front of the right pulmonary veins otherwise there is no bleeding.

The right index finger is inserted into the right atrium through the auricle, and the type, size and location of the defect is determined. An ordinary blunt probe is bent in a suitable curve. Its tip, placed at the upper end of the cleavage with slight pressure disappears into the tissue. Almost by its own weight and with the finger in the atrium, the probe is guided in the tissue along the lower edge

(7) Acta chir. scand. nav. 109:188-196, 1955.

of the defect until the tip appears on the surface at the lower end of the cleavage, in the triangle of fat located between the right and the left atrium and the coronary sinus. Force should not be used.

The tip of the probe is caught with a hemostat. An oiled silk suture no. 10 is tied to the probe, which is then pulled back, carrying the suture. The two ends of the suture are tied over a piece of gelatin sponge placed in the bottom of the cleavage. As the suture is gradually pulled tight, the finger in the right atrium feels the defect becoming smaller and smaller and finally close. No more tension should be applied. The finger is withdrawn from the heart and the auricle closed. The pericardium is only partially closed. Finally the pleural cavity is drained and the chest sutured in layers.

The advantages of the technic are (1) the established septum is located in the normal septal plane and consists of normal atrial septal tissue; (2) neither the right nor the left atrium is altered in shape or function; (3) multiple defects present no special problem; (4) no sutures or other foreign bodies are left exposed inside the heart; (5) no needle is used, and the blunt probe eliminates the danger of piercing the aortic wall; (6) ordinary anesthesia is used; (7) only a right standard thoracotomy is needed; (8) the probe slides parallel to the described course of the bundle of His with minimal risk of damage, and (9) mortality has been zero in dog experiments and clinical cases. The procedure was used in six patients. All patients catheterized post-operatively had complete closure of the defect, and the pressures returned to normal within two weeks.

**Evaluation of Mitral and Aortic Valvular Disease by Left Heart Catheterization** was made by George Hugh Lawrence. Herbert B. Zimmerman, Bernard A. Bercu and Thomas H. Burford<sup>8</sup> (St. Louis) in 25 candidates for cardiac surgery. Four had tight mitral stenosis, eight moderate stenosis and regurgitation and two little mitral valve involvement despite severe subjective symptoms. Nine had marked regurgitation. Two of four patients with aortic stenosis had associated mitral valve disease. All the lesions were verified at operation or autopsy except in seven patients with mitral regurgitation or minimal disease who were not operated on and in two with pure aortic stenosis, one of whom was awaiting surgery. No significant disparity was noted between the valvular lesion as predicted by pressure readings and that found at operation.

No mortality or significant morbidity was encountered.

(8) Surg., Gynec. & Obst. 101:558-562, November, 1955.

Operation often revealed a small amount of serosanguineous fluid in the pericardium. No clinically recognizable pneumothorax, hemothorax or cardiac tamponade was noted. In one patient, a small segment of polythene catheter sheared off and remained in the left ventricle. It could be palpated at valvotomy but not extracted, and it produced no recognizable deleterious effects. During catheterization, inadvertent entry of the needle into the left ventricle in one patient and into the pulmonary artery in two others caused no sequelae.

The normal auricular pressure curve is made up of three positive waves. The A wave is caused by auricular systole. The C wave is caused by rising pressure in the ventricle with onset of ventricular systole, the pressure being transmitted to the auricle through the mitral valve. The negative wave following the C wave, the so called "descent of the base," is produced by negative intra auricular pressure caused by ejection of blood from the ventricle and the drawing caudad of the atrioventricular septum as the ventricle contracts. The third positive wave, the V wave, is caused by inflow of blood into the auricle from the pulmonary veins. Decline in pressure following V waves occurs when the mitral valve opens. During ventricular diastole, end diastolic pressures in the auricle and ventricle are equal.

In a patient with severe mitral stenosis and little or no regurgitation, the auricular pressure curve is similar to the normal. Descent of the base is maintained and the rise of the V wave minimal, not ascending above the C wave. The diagnostic feature in mitral stenosis is the high end diastolic pressure gradient between the auricle and ventricle. This gradient can be recorded continuously as the catheter is withdrawn from the ventricle to the auricle. In absence of measurements of cardiac flow, the greater the pressure gradient across the mitral valve during diastole, the greater the stenosis. In patients with a tight mitral stenosis the gradient was over 15 mm Hg. In four patients with combined aortic and mitral lesions, auricular tracing showed characteristics of the mitral lesion. Auricular and diastolic pressure and auriculoventricular pressure gradient were high.

Characteristic diagnostic features in mitral insufficiency are absence of descent of the base following the C wave and the high V wave which begins somewhat earlier than nor-

mal and rises higher than the C wave. In patients with marked mitral insufficiency, the difference in pressure between the C and V waves has been over 12 mm Hg. The auriculoventricular pressure gradient was low, 0.7 mm Hg.

Between these extremes are patients with variable scarring of the mitral valve and all combinations of mitral stenosis and insufficiency. In these patients, left auricular puncture is of greatest value in predicting amount and type of valve deformity.

In presence of aortic lesions, left heart catheterization is desirable. As there is little correlation between intensity of murmur and degree of aortic stenosis, the systolic pressure gradient across the aortic valve is an important indication of obstruction. Four patients with aortic stenosis had gradients over 70 mm Hg. In one instance, the auricular curve was normal and identical auricular and ventricular end diastolic pressures indicated presence of a normal mitral valve. Giant A waves seen in two patients were similar to the large right auricular A waves seen in pulmonic stenosis.

**Studies in Mitral Stenosis. VI. Pulmonary Vessels in Mitral Stenosis.** Knut Bulow, Gunnar Björck, Oliver Axén, Hans Krook, Helge B. Wulff and Sten Winblad<sup>9</sup> (Malmö, Sweden) evaluated pulmonary function and anatomy in 50 patients undergoing surgery for mitral stenosis by preoperative angiopulmography, cardiac catheterization, chest x-rays and biopsy of the lung during surgery. Six patients had exploratory cardiectomy only and 32 had valvulotomy, mostly digital commissurotomy. There were seven operative deaths. Lingular biopsies were made in 38.

Five of the patients who died had pulmonary complications, three had marked atelectasis or unilateral total pneumothorax, two moderate atelectasis and all but one clinical signs of ventilatory difficulty. Of 17 living patients with grave postoperative complications, 11 had pulmonary disturbances. The main pulmonary complications were atelectasis, pleural effusions and pneumonic infiltrations. None of the surviving patients had pulmonary edema. Severity of the complications increased with increased duration of the operation.

The lingular biopsy revealed vascular changes in nearly two thirds of 38 patients. Of the 33 who underwent both

(9) *Am Heart J* 50:242-259 August 1955.

lingular biopsy and angiopulmography, 23 had various degrees of pathologic vascular changes. Pathologic angiograms were more frequent in the group with concomitant histologic changes. Radiologic changes are found more often than histologic changes and probably at an earlier stage. Angiopulmography is a better clinical method of investigation than biopsies because it reveals changes in the large and medium sized vessels. Histologic analysis shows the changes in the minute arteries and capillaries. There is a fairly good correlation between histologic and angiopulmographic findings despite the fact that they involve different parts of the lung. Chest x rays yield less information than angiopulmography. Pulmonary complications were more frequent in the patients in whom biopsy was made and for this reason resection has been abandoned.

Cardiac catheterization and arterial puncture before operation gives valuable information on pulmonary vascular resistance, cardiac index and arterial oxygen saturation level. Markedly increased resistance in the pulmonary vessels is more often found in patients with structural lung changes but there is no actual correlation between pathologic pulmonary vascular resistance and structural changes as a whole. Most patients with a low cardiac index had severe structural changes. A low arterial oxygen saturation was found in some patients with such changes. Severe structural changes were found in patients who had pulmonary symptoms for many years in those in a lower pulmonary functional class and in the higher age groups.

There was no marked difference in operative result in surviving patients between the group with and the group without structural changes.

**Surgical Treatment of Mitral Stenosis.** Conclusions Regarding Diagnosis, Indications, Technic and Prognosis of Commissurotomy Based on Direct Investigation are presented by Theo Hoffmann<sup>1</sup> (Paris). Successful commissurotomy depends on the following clinical and technical considerations: (1) Commissurotomy may be impossible because a funnel shaped stenosis (type III) exists or the annule is too small or completely thrombosed. Substitute approach directly through the ventricular wall is more difficult and more dangerous though it sometimes yields successful

(1) Deutsche med. Wchnschr. 81:1926 Jan. 6, 1956.





into the mitral opening. With this blunt instrument, the valve can be dilated to normal or nearly normal proportions. It is available in several sizes for adaptation to the individual case, which is important because a small auricle is another factor that can prevent insertion of the finger.

Mortality can be reduced practically to zero if operation is confined to only purely edematous mitral stenosis in young individuals or if only the finger is used. Experience shows, however, that in most mitral stenosis, dilatation with the finger is not sufficient and that an instrumental procedure is required to produce satisfactory results. Attempt to achieve a functional widening in every case carries increased risk, as the clinical statistics since the use of the Dubost dilator demonstrate. Nevertheless, use of this instrument is increasing.

Among the 155 patients in whom the dilator had to be used, the instrument was responsible for six deaths. In three, the chamber wall was perforated, in one, a papillary muscle was ruptured and in two, the left ventricle was lacerated. There were five postoperative deaths: one hemopericardium, one embolus of the aortal bifurcation, two heart failures, and one pulmonary embolism. Thus the total mortality was 7%. If this instrument had not been used, surgical mortality would have been lower, but effective clinical results would have decreased.

The literature shows definite correlation between degree of dilatation and quality of results. With dilatation of over 2 fingerbreadths, results are good in 85% up to 1½ finger breadths, in 67% and to 1 fingerbreadth, in only 11%. With type I stenosis, good results can be anticipated after commissurotomy (only 11% fair or poor results). Type III carries a poor prognosis (61% unsatisfactory), and in type II, about 25% of results are fair or poor. However, these statistics include a large proportion of patients operated on before the problem of instrumental commissurotomy was solved. The results indicate the importance of proper evaluation of cases before operation.

Commissurotomy promises to become increasingly important, as clinical results accumulate. Even though the procedure cannot be expected to restore a completely normal mitral valve, follow-up of two to five years indicates that results are definitive and permanent.

**Mitral Valvotomy: Follow-up of 45 Patients for Three Years and Over** (to six years) is reported by Charles Baker, Russell Brock and Maurice Campbell<sup>2</sup> (Guy's Hosp, London). A year after operation 38 had good or excellent results, at the end of three years, 11 of these had deteriorated, leaving 27 with satisfactory benefit. Some patients had maintained improvement for four and five years and were leading active lives. Addition of some patients less completely followed showed 50 patients operated on three years or more ago with good or excellent results, 38 (76%) were still as well after three years, and 12 had lost ground. Four of the latter regressed completely, and two of these died. Of 19 followed four years, 15 maintained improvement, 2 lost much and 2 lost all improvement.

Size of heart, degree of disability and presence of auricular fibrillation preoperatively apparently do not influence the result during the first three years though fibrillation increases operative risk. Results were better when, at operation, the valve was less than 1 cm in diameter. When the surgeon could not produce an opening as large as 2 cm or when gross incompetence was present, results were not good. When a full opening or one over 3 cm could be produced, 1 poor and 17 good results ensued. When valve size was intermediate, 2-3 cm, results were intermediate. Mitral regurgitation before valvotomy does not always prevent satisfactory outcome but reduces proportion of good and increases that of fair results. Regurgitation (associated with calcification of the valve) was produced by valvotomy in 6 of 45 patients, in 3, results were poor or only fair and in 3 apparently satisfactory. Successful valvotomy never failed to reduce pulmonary hypertension and, in general, the greater its degree the better the chance of good results.

Temporary fibrillation after operation when sinus rhythm is restored spontaneously or with quinidine does not seem to influence the outlook. In three patients in whom fibrillation occurred postoperatively and normal rhythm could not be restored, results were poor. Of 18 with fibrillation before operation, 14 maintained good or excellent results. Onset of atrial fibrillation is to some extent a test of the heart's capacity. Unless the heart was able to stand this reasonably well, the patient might have been regarded as too ill for

operation Loss of improvement from operation when atrial fibrillation occurs later indicates that margin of benefit conferred was not great and suggests that the valve has restenosed

Prognosis in a young patient depends mainly on whether or not further cardiac damage occurs from rheumatic infection This is less true in older patients but still has some relevance There is no correlation between presence of Aschoff bodies in the auricle and clinical evidence of rheumatic activity and subsequent course Three patients, of whom one died and two had second operations, had restenosis, more likely due to reinfection than to fibrosis from stress

Physical signs and improvement in ECG or x ray after operation give a better indication that the result is likely to be lasting than the symptoms and increased capacity of the patient In the present series, 2% of patients lost all improvement during the first year, 6% during the second, 10% during the third and about 15% during the fourth, twice as many lost some improvement This result, though not ideal, is better than the estimate made the previous year and may become better as more patients are followed It is unlikely that improved selection and surgery will ever prevent all progressive deterioration, for the hearts being dealt with have been damaged by rheumatic infection These first 45 patients were selected because of bad prognosis, and some were operated on before valvotomy technique was perfected Even those who did not maintain initial improvement had benefit of increased or normal activity for a year or more That a second operation can be done on some patients if restenosis occurs emphasizes need of careful and thorough follow up

► [This report and the one following are very timely in answering a question that is often asked about the long range results of this operation The results reported by Brock and his associates as well as those by Glover seem very good but probably as techniques improve the results will also—Ed]

**Present Status of Patients Subjected to Mitral Commissurotomy Five or More Years Ago** Intracardiac surgery for acquired valvular disease is now a well established and highly successful adjunctive and definite form of treatment Commissurotomy for mitral stenosis is probably the best established of the operations The first 50 consecutive pa-

tients with mitral stenosis subjected to commissurotomy by Robert P. Glover<sup>3</sup> (Philadelphia) have been followed for 5-6½ years. In 40% there was a definite history of rheumatic infection. Each of the 50 was suffering from cardiorespiratory functional incapacity, 54% had one or more bouts of congestive failure, 46% had a history of gross hemoptysis and 12% had recovered, with some residual damage, from arterial emboli. Three patients died within the first post-operative month, an operative mortality of 6%. Each was in an advanced obstructive phase of the disease and had chronic atrial fibrillation. The cause of death was inadvertent production of too much valvular insufficiency in two and surgical shock in one. Six other patients died within three years. All were in an advanced stage of their disease, and had extensively calcified valves whose leaflets were fibrosed, indurated and motionless. Death was the result of pre-existing disease, which had led to irreversible cardiopulmonary, hepatic and renal conditions only temporarily improved by relief of valvular obstruction.

Of the original 50 patients, 41 were alive five or more years after surgery. Of these, at least 30 were in better condition and living a more nearly normal life than before surgery. Altogether 20 were in excellent condition, 16 improved, 5 unimproved and 9 dead. Objective signs of improvement following mitral commissurotomy corroborated the subjective findings. In 10 the heart size was smaller, in 26 the same and in 5 larger than preoperatively. In the years preceding surgery this organ had become progressively larger.

Of the 41 living patients, 27 underwent cardiac catheterization before surgery and 14 of these again 1 to 5 years later. In three patients, all recatheterized over five years after surgery, initial pulmonary artery pressures had dropped from 81/31, 105/24 and a mean of 72 mm Hg to 24/6, 23/4 and a mean of 14 mm Hg, respectively, representing a return to normal levels. Electrocardiographically, ultimate changes following surgery showed a definite return toward normal in about 50% of the cases. On the basis of cardiac murmurs alone, no definite conclusions concerning the patients can be reached. Only 4 of the 41 had heart sounds free from murmurs. A mitral systolic murmur of

varying degrees was present in 14 patients who did not have it before surgery. There have been no emboli postoperatively, in contrast to an incidence of 12% before surgery. A definite activation of the rheumatic state occurred in 19.5%, but in none of these has there been any observed effect on the anticipated result of surgery.

**Factors Influencing Late Results of Mitral Valvuloplasty for Mitral Stenosis** Laurence B. Ellis and Dwight E. Harken<sup>4</sup> (Boston) report on their first 500 patients. Mean follow-up was 22 months. There were 58 operative deaths, 2 patients were lost to follow-up and the other 440 were evaluated.

None of the patients was in group I—without significant symptoms, 13 were in group II—without progressive symptoms, most (342) were in group III—progressive symptoms, and 145 were in group IV—cardiac invalids. In the first 100 patients in groups II and III, mortality was 14%, whereas in the last 100 it was less than 3%. In group IV, operative mortality remained at 20–25% throughout.

Moderate to marked improvement occurred in 78%, 22% were unchanged or worse or died. Older patients did not do as well as younger. Patients with auricular fibrillation were not so often improved as those with normal sinus rhythm. None of the patients had a severe grade of associated valvular disease but those with aortic diastolic or systolic murmurs, as a group, did less well than those without.

The greatest problem was estimation of mitral insufficiency. A mild degree of insufficiency did not affect ultimate good prognosis but with greater insufficiency, the patients did less well. Most of these patients had significant mitral stenosis which was corrected.

Adverse factors were age over 40, auricular fibrillation, some associated aortic valve involvement, associated mitral insufficiency of moderate degree or more, preoperative valve size of more than 1 sq. cm., postoperative valve size of less than 2.5 sq. cm. and calcification of the mitral valve. If none of these factors was present, 96% of the patients were improved. If any five were present, only 50% were benefited.

All patients with mitral stenosis and auricular fibrillation are liable to peripheral emboli, though this is more likely if one or more emboli has previously occurred. Of 79 pa-

tients with previous emboli, 71 were fibrillating at operation, and 17 (24%) of the 71 had an embolus during surgery, compared with over-all percentage of embolization of 5.6 in group III and 16 in group IV. Among a succeeding 300 patients, incidence was reduced to 10% in those with pre-operative emboli and to a total incidence of 2.8% in group III and 11% in group IV. Danger of late peripheral emboli was low. Only 6 of 442 surviving patients had emboli though more than half were fibrillating. Of a succeeding 300 patients, only 2 had late emboli. Operation significantly reduced incidence of emboli.

Changes in objective clinical findings, heart size and configuration, murmurs and ECG's in 106 patients were not consistent or striking and were not correlated with improved exercise tolerance.

**Mitral Commissurotomy.** Present Status Based on Personal Experience in 400 Cases is evaluated by F. D'Allaines and Ph. Blondeau<sup>5</sup> (Paris). Patients without functional disturbances should not have surgery. Early in the series, patients over age 50 were refused operation but later, criteria were extended to include older patients with mitral stenosis and right ventricular insufficiency or with polyvalvular lesions if mitral stenosis was a predominant clinical feature. Mild fever, complete arrhythmia and peripheral embolism are not contraindications. In mitral insufficiency, indication for operation may be questionable, and each patient must be evaluated individually on the basis of radiologic and ECG findings and at times on determination of left ventricular pressure during operation.

Technical problems in commissurotomy have not all been solved. Because of wide selection of cases, the authors encountered surgical difficulties in about two thirds of the operations. Principal problems are penetration into the auricle and in performing the commissurotomy itself. When the auricle appendage is small, which is almost impossible to predict preoperatively, the auricle should be penetrated directly. Thrombosis of the auricular appendage is easy to treat, that of the auricle difficult and dangerous. A very wide commissurotomy is recommended. A special mitral dilator is useful for this but demands delicate manipulation and may be dangerous in unskilled hands. An ECG made during

operation permits foreseeing certain cardiac difficulties before they appear, and excitable hearts can be protected against rhythmic disturbances. In general, prophylaxis against rhythmic instability is accomplished with hexamethonium, injected as soon as the patient is placed on the operating table, and sparteine sulfate, injected when the heart is uncovered, and repeated if necessary. Estimation of pressures in the auricle and left ventricle permits definite evaluation of the result obtained.

Seven patients died on the operating table, three of posterior ventricular injuries caused by the metallic dilator. During the first two postoperative weeks 22 patients died, a total operative mortality of about 7%. Late results are somewhat difficult to evaluate as at least six months are necessary to judge the actual result in patients with immediate results apparently favorable. Among 150 patients re-examined more than six months after commissurotomy, functional results were excellent in 38% and good in 28% (total about 66.5%), fair in 14.5% and poor or mediocre in 19%.

True recurrence of mitral stenosis appears to be extremely rare following complete and satisfactory commissurotomy. Most patients having progressive symptoms after some months of improvement had faulty, incomplete commissurotomies. Numerous secondary operations were performed in these patients, in most of whom incision of the atrial wall was necessary to achieve satisfactory results. As this increases the hazard of operation, these procedures should be performed only in special centers. The principal danger in current mitral surgery is that from poorly executed, incomplete operations, which also preclude definitive evaluation of results.

Discrepancies between Subjective and Objective Responses to Mitral Commissurotomy were analyzed in 31 patients (60% of a series) 4-38 months after operation by Gordon G. Bergy and Robert A. Bruce<sup>6</sup> (Univ. of Washington).

Although 29 of 31 patients considered themselves better as a result of mitral valve surgery, 16 had higher, 6 the same and 7 lower physical fitness index scores, a correlation of

(6) New England J. Med. 253:887-891 Nov. 24, 1955

only 55%. One patient who said he was the same had a lower physical fitness index postoperatively, whereas one who gave no answer (and really believed she was worse) had a higher index. Most patients still needed some form of medical therapy, and half still needed daytime periods of bed rest. These two facts, in contrast to subjective opinions, correlate with objective findings on physical examination and standard exercise tolerance tests. Hence, for some patients, "better" connotes a change in attitude toward their disease and disability, rather than improvement in cardio-respiratory function.

The most important effects of surgery were decreased intensity and frequency of dyspnea and fatigue after effort, corroborated by the fact that 15 patients were able to work full time without limitations, in contrast to only 3 preoperatively. There were corresponding changes in symptoms in relation to standard work load of exercise tolerance test, with increased endurance, slower heart rate, higher systolic blood pressures during exercise and higher physical fitness indexes. A few patients, despite improvement in attitude, continued to have specific job limitations and were physically unable to participate in fairly sedentary recreational activities because of diminished cardiac reserve. Possibly these patients have chiefly myocardial insufficiency, which may be manifested by heart failure, in part due to carditis, or the postcommissurotomy syndrome often associated with rheumatic heart disease. These factors may account for the apparently poor correlation between functional results and type and degree of valvulotomy obtained.

They may also provide understanding of the similarity of improvement in exercise tolerance between patients operated on and those not operated on who have survived for a year or more. Mean physical fitness index increased from 9.3 to 12.0 in the former and from 9.4 to 12.1 in the latter (here reported). Difficulties in evaluation probably will persist because of presence of both mechanical block and myocardial insufficiency.

Surveys based on information obtained from patients may not be entirely reliable when not controlled. Ultimate appraisal of this type of therapy must await passage of time. Only when all patients (those operated on and those not



operated on) are followed to death, will it be possible to determine whether the natural history of the disease and longevity have been significantly altered

► [This study is very important and in general it agrees with one published by Soloff and Zatuchni (JAMA 154 673 676 Feb 20 1954) Bergy and Bruce have devised what they call a physical fitness index for the objective evaluation of results The formula is

$$PFI = \frac{\text{Endurance} \times \text{respiratory efficiency} \times 100}{\text{Cumulative 3 minute recovery heart rate}}$$

For details the original article should be consulted Perhaps the previously mentioned opinions of the surgeons are too optimistic—Ed]

**Reoperation for Mitral Valve Disease** is recommended by Ivan D Baronofsky Craig Borden Ralph E Smith and Joseph L Sprafkin<sup>7</sup> in three types of cases i.e., possible recurrence of mitral stenosis giant atrial thrombi or preponderant regurgitation at initial exploration

**TECHNIC**—Adhesions between pleural surfaces are broken down as usual The usually adherent pericardium is opened posterior to the phrenic nerve and the left ventricle and atrium completely exposed by careful blunt and sharp dissection Cautious examination discloses an elevated area on the atrial wall which is the remnant of appendage remaining from the previous operation By slight tension exerted on an Allis forceps at its apex and blunt dissection with a Luettner sponge a fair area of appendage can be obtained and tiny strands of fibrous tissue trapping it are easily cut Fat surrounding coronary vessels lying in the atrioventricular groove can be dissected toward the ventricle for a surprising distance (to 2 cm) without disturbing vessels within it giving much added space for the purse string suture of 0 silk which is placed around the dissected appendage and threaded through a Rumel Belmont tourniquet The carotids are clamped temporarily and a Satinsky forceps is placed at the lowest level of the base of the appendage by lifting gently on the purse string suture and then placing the clamp at or even below the suture level A small incision (about 1 cm) is made in the atrial wall protruding above the closed clamp and parallel to the axis of its jaws The clamp is momentarily loosened to check for blood leakage through the incision as sutures placed at previous operation usually constrict the appendage internally with no external evidence If blood is obtained the incision is lengthened just enough to admit the index finger

Two Allis forceps are placed at the edges of the incision and the finger inserted as an obturator while the Satinsky clamp is released The finger is then gently forced through the constriction as one would dilate a constricted colostomy Careful and deliberate manipulation finally puts the finger in the atrium proper and the valve is fractured If necessary a knife may be inserted with the finger after dilatation is completed After valvulotomy has been accomplished reduction in atrial pressure relieves the tension on the atrial

wall and more of it can be brought beyond the Satinsky clamp edges as the finger is removed. This is done by gently pulling upward on the Rumel tourniquet and the lateral wall of the atrium as it is grasped by the index finger within the heart and the thumb of the same hand, while slowly sliding both fingers in an upward direction. The incision is then oversewn with silk until complete hemostasis is assured. The purse-string suture is not tied tightly but is removed or fixed loosely in place. The pericardium and chest are closed.

When constriction presented by the suture placed at first operation completely obstructs the entering finger, a straight Kelly forceps is boldly inserted in the center of the atrial incision. When bleeding is obtained, the forceps is opened quickly to begin dilatation and the finger is inserted as above.

In three of five patients, good results followed second operation for mitral stenosis, with great improvement in exercise tolerance. In one patient, results were only fair immediately after operation but improved considerably later. One patient died at operation because a piece of calcium plaque broke loose from the edge of the valve and entered the systemic circulation. At autopsy, calcium was found in the anterior and middle cerebral arteries.

**Digital Exploration of Cardiac Chambers and Mitral Murmurs** are discussed by R. Lutembacher<sup>8</sup> (Paris). Anatomic examination of the mitral cone, revealing rigidity, deformities and, at times, persistence of a calcified orifice, suggests that mitral regurgitation should be observed in all types of rigid stenosis. Mitral regurgitation is often detected by presence of a systolic murmur, but this may be absent. To explain its lack, authors who believe that mitral regurgitation is always present with uncomplicated stenosis contend that the murmur is inaudible. Because of failure to detect murmurs by auscultation, kymography has been recommended to demonstrate systolic expansion of the left auricle. In Lutembacher's experience, however, this is not a reliable method of proving auriculoventricular regurgitation.

Digital palpation, during commissurotomy, may yield findings which disagree with clinical observations, i.e., regurgitation may be found in cases without audible systolic murmur, and vice versa. These discrepancies may be explained by the fact that the surgeon's manipulations during exploration may, in some cases, cause an existing regurgitation to disappear, and in others, may cause it. In uncomplicated stenosis without significant ventricular dilatation,

(8) *Presse méd.* 63:801-804, May 25, 1955.

slight weakness of the muscular articulation, resulting in loss of precise contact with the mitral cone, is enough to cause mitral murmur. Under such conditions, the surgeon's finger pushing the mitral cone slightly could replace it on the muscular joint and pre-existing mitral regurgitation would disappear. Conversely, lateral movements impressed on the mitral cone could cause it to see-saw and be thrust out of gear with its muscular connection, thus giving rise to regurgitation that was previously nonexistent.

In efforts to explain apparent discrepancies among anatomic, clinical and surgical observations it is important that lesions be examined carefully, with attention not only to deformity of the mitral cone but also to muscular connections. The tightness of the orifice is assured as long as contact is maintained between the valvular apparatus and the muscular articulation formed by the pillars; these are the two structures that control occlusion of the orifice.

Myocarditis breaks this contact by dilatation of the filling channel and thus intervenes in the pathogenesis of mitral systolic murmurs, i.e., myocardial murmurs of stenosis or mitral insufficiency without valvular lesions. Appearance of murmur is not attributable to distention of the orificial ring (an outmoded concept of functional murmurs due to dilatation), but rather to lack of contact and "meshing of gears" of the muscular connection formed by the pillars with the valvular joint.

**Surgical Correction of Tetralogy of Fallot. Results in First 100 Cases Six to Eight Years after Operation** are reported by Willis J. Potts, Stanley Gibson, Edward Berman, Harvey White and Robert A. Miller<sup>9</sup> (Children's Memorial Hosp., Chicago). In this series, four patients required second operations to relieve recurrent cyanosis. The anastomotic channel closed following anastomosis on the left side in one patient and on the right side in two.

Results six to eight years after operation were good in 68%. These children showed little or no visible cyanosis when at rest and slight cyanosis after exercise. They were able to attend public school, play, ride bicycles and do everything suitable to their age except violent exercise. One boy in this group, now 17, operated on at age 9, had an excellent result clinically, but x-ray films showed an aneurysmal dilatation

of the left pulmonary artery and his future is considered uncertain. Another child was well for six years after operation but had recently recovered from what the family physician considered bacterial endocarditis. This was the only known case of late bacterial invasion of vessels.

Results were classified as fair in 16 children who were moderately handicapped. These children were found to tire easily on moderate exertion. Some had persistent mild cyanosis at rest, but all became cyanosed on exertion or when fatigued. All were excused from gymnastics. However, all showed moderate to marked improvement over their condition before operation. All but one continued to have the characteristic continuous murmur.

One girl, 13, had a poor result and remained severely handicapped. Because she had been bedridden two years, a large anastomosis, 6 mm in diameter, had been made, which promptly relieved all cyanosis. After a vacation in Yellowstone Park, in which excessive exercise was allowed, her heart became tremendously enlarged, and subsequently heart failure developed several times. During the last year, heart enlargement had decreased from 125% to 60%, an aneurysm of the left pulmonary artery had developed and a diastolic phase of the murmur had disappeared. She appeared to be free from cyanosis but obviously prognosis was poor. One patient who had two operations had only temporary improvement each time.

Fourteen patients died, five improved after operation but died later, and hospital mortality was 9%.

Although these children all had about the same operations, the degree of cardiac enlargement afterward varied considerably. Presumably, the size of the anastomoses varied despite careful measurement, or the anastomosis increased in size more in some patients than in others. Variation in uncorrected pathology inside the heart may also be a factor. Heart size after such operations is undoubtedly an important factor in ultimate prognosis but is not a guide in early results, i.e., in six to eight years. What the heart muscle unhampered by disease of its vessels, can do is constantly astounding. Aside from six patients who developed a pattern of combined heart strain, ECG changes over the years after aortic pulmonary anastomosis revealed few significant changes.

► [Like the long term follow-up studies on mitral commissurotomy already abstracted, this report by Potts is timely and it gives the kind of information that is often sought—Ed]

**Diagnosis and Treatment of Tricuspid Atresia** are described by William L. Riker and Robert Miller<sup>1</sup> (Children's Mem'l Hosp, Chicago), with a report on 51 patients. The

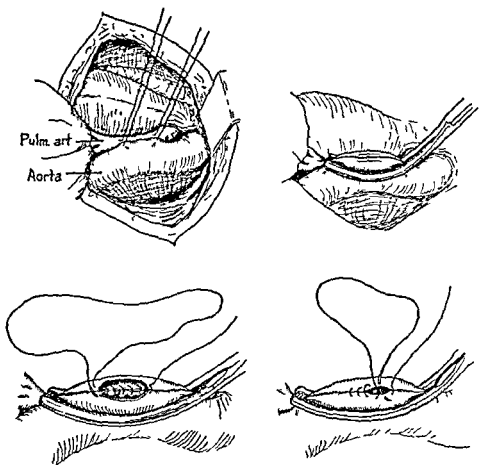


Fig 56 (top left) —After pulmonary artery and aorta are freed two traction sutures are placed 1 cm apart in two arteries pulling them up and together.

Fig 57 (top right) —Curved coarctation clamp placed on two vessels occluding and approximating their lips.

Fig 58 (bottom left) —Details of suturing posterior portion of anastomosis with continuous suture of 6/0 silk.

Fig 59 (bottom right) —Details of suturing anterior portion of anastomosis.

(Courtesy of Riker W L and Miller R. Surgery 38:886-902 November 1955)

pathology consists primarily in complete atresia of the tricuspid valve area with an interatrial septal defect. Four patients had type A variation (tricuspid atresia with pulmonary atresia and no interventricular septal defect), 17 had type B variation (tricuspid atresia with an interventricular septal defect through which some blood was able to enter

the rudimentary right ventricle and pass out into the lungs) and 1 had type C variation (tricuspid atresia with transposition of the great vessels)

Patients were under 3 years old or died untreated in 80% of the cases. Survival into the second decade is rare. Almost all had cyanosis from birth, dyspnea, weakness, failure to gain weight and decreased exercise tolerance, and some had brief episodes of unconsciousness. Clubbing of fingers and toes, if present, was only slight. A loud, harsh systolic murmur was usually heard best in the third intercostal space to the left of the sternum. A systolic thrill was palpable. Cardiac enlargement was found in only one patient with congestive failure. The liver was enlarged in 60% but pulsating in only 10%. Moderate polycythemia, averaging 20 Gm hemoglobin, was found.

X-rays indicated a normal heart size in 60% and only slight enlargement in the rest. The heart was transverse, with a prominent, rounded left border and without the concavity in the region of the pulmonary artery segment so characteristic of a tetralogy of Fallot. Vascularity of the lung fields was decreased. Fluoroscopy indicated absence of right ventricular enlargement.

ECG's revealed left ventricular hypertrophy. A ventricular complex consisting of a Q-S, or a small R and deep S wave in the right-sided chest leads was often the only abnormality in young infants. In older children, typical left heart strain with peaked P waves in lead II was constant. Angiocardiograms and catheterization studies are seldom necessary.

The aim of treatment is to increase blood flow to the lungs; correction of the atresia itself is not possible. The recommended operation is aortic-pulmonary anastomosis (Figs 56-59), particularly in patients under 3. It should be performed immediately when symptoms are increasingly severe, because of the high mortality rate. When symptoms are less severe, operation can be deferred until patients are a little older.

Of 16 patients not operated on, 15 died. Thirteen of these were under 6 months, and most were in poor condition with spells of unconsciousness and periods of apnea. None of the 35 patients who underwent surgery died during the procedure. Five died from 1½ hours to 14 days afterward, three

of heart failure and two of pulmonary infarcts secondary thrombosis at the anastomosis. Of the 30 patients discharged from the hospital, 2 had poor results because of persistent heart failure. There were five late deaths, two attributable to a combination of the disease and the operation, two unrelated causes and one to septicemia (vegetations found around the anastomosis at autopsy). Of 25 patients followed for four months to eight years, 19 had good results, 5 fair results and 1 a poor result. X-rays revealed increased vascularity of the lung fields and some prominence of the pulmonary artery segment in patients with good results. Moderate cardiac enlargement, mostly of the left ventricle, occurred in 60%.

**Diagnosis of Aortic Stenosis.** Viking Olov Björk and Gunnar Malmström<sup>2</sup> (Stockholm) state that the paravertebral method of left heart catheterization is excellent for determining the pressure gradient across the aortic valves preoperatively in patients suspected of having aortic stenosis.

**TECHNIC.**—A 20 cm needle, internal diameter 1 mm and external diameter 1.5 mm, is introduced paravertebrally from the right side. A paravertebral introduction without passing lung tissue is possible only when the left atrium is enlarged. However, complications are not encountered when the needle passes directly through the periphery of the lung. A point in front and at the back in a straight line through the left atrium is marked on the patient during X-ray study. A point 7-10 cm lateral to the midline, usually above the ninth rib on the right side, is chosen. Local anesthesia is used in the skin, muscles and pleura. Once the left atrium is entered and its pressure measured, a fine soft plastic catheter (0.5 mm inner diameter) is introduced through the left atrium and into the left ventricle. At the same time, simultaneous pressure measurement in the left ventricle and brachial artery; the catheter is passed out into the aorta. Pressure measurements are then made when the catheter is withdrawn from the aorta to the left ventricle. The catheter may be passed from the left ventricle out into the aorta despite considerable aortic stenosis. Pressures are recorded with a Warburg-Hansen capacitance manometer.

This procedure has been used in more than 100 cases. Syphilitic aortitis is the only contraindication to its use. It can also be used in cases with constrictive pericarditis and myxoma in the left atrium.

In aortic stenosis, the indication for operative treatment of the stenosis *inter alia* should depend on the pressure gradient across the aortic valve. A systolic pressure gradient

of 50 mm Hg across the aortic valves may be considered an indication for operation on an isolated aortic stenosis. When there is a combination of mitral and aortic stenosis, a systolic pressure in the left ventricle, exceeding the systolic pressure in the aorta, of more than 30 mm Hg is an indication for operation on both valves at the same time. In these cases of aortic stenosis there had been a significantly increased diastolic pressure in the left ventricle (222/12 mm Hg and 227/12 mm Hg) and consequently an elevated left atrial pressure. In the beginning of diastole the pressure was 12 mm Hg and in the end of diastole, 20 mm Hg in the ventricle. It is not known in what stage of development of human aortic stenosis the left ventricular diastolic pressure will increase significantly. Experimentally, there is no significant elevation of the ventricular initial tension if constriction of the aortic orifice is less than about 40%.

**Postoperative Myocardial Infarction. Report of 25 Cases** is presented by Fred Wasserman, Samuel Bellet and Robert P. Saicheck<sup>3</sup> (Grad Hosp of Univ of Pennsylvania). From Aug 1, 1948 to Aug 1, 1954, 37,000 operations, 60% major, were performed. Postoperative myocardial infarctions occurred in 21 patients after major and in 4 after minor operations. Average age of the 10 men and 15 women was 64½ years. Heart disease was present preoperatively in 19, of whom 7 had hypertensive cardiovascular disease, 6 arteriosclerotic cardiovascular disease, 5 hypertensive and arteriosclerotic heart disease and 1 rheumatic heart disease (mitral and aortic). Preoperatively, the anginal syndrome was present in eight, and two showed ECG evidence of previous myocardial infarction. Pulmonary fibrosis and mild diabetes mellitus were present in one each. Of 10 patients seen preoperatively by medical consultants, 1 was considered a good risk, 5 fair, 1 poor to fair and 3 poor.

Of the 21 given general anesthesia 7 received muscle-relaxing drugs also. Two received spinal and two local anesthesia. Average duration of surgery was 1 hour and 50 minutes, with a range of 30 minutes to 6 hours. The operation was abdominal in 17, pelvic in 3, thoracic in 1, orthopedic in 2 and in other regions in 3, 1 patient having both chest and abdominal operations.

A decrease in blood pressure of 40 or greater systolic

(3) New England J Med 252:967-974, June 9, 1955



and 20 or more diastolic, lasting 5-30 minutes, occurred in 12, and 6 had slight blood pressure depression. In some patients, it was difficult to determine exactly when infarction occurred. It occurred on the day of, or within the first seven days of, surgery in 92% and in the second postoperative week in the others. Only eight patients had the typical severe precordial pain or substernal pain with a sensation of substernal oppression or constriction, and four of these had persistent hypotension. In four others, the pain was located in the left shoulder, right side of the chest or high in the midepigastrium, two of these had hypotension. Significant hypotension without pain was present in 10, and 3 had neither pain nor hypotension. Hypotension was a more important manifestation than pain and was found in 64%. Arrhythmias occurred in three patients. Five patients died: three of infarction, in the other two, other serious disease contributed to death. The ECG changes were characteristic or suggestive of myocardial infarction.

Though emergency surgery should not be denied to any patient, if elective surgery is planned for patients over 50, a detailed study is essential to decrease the operative risk. Cardiac enlargement, hypertension, previous myocardial infarction, angina pectoris, conduction disturbances, congestive heart failure, aortic stenosis, syphilitic heart disease and rapid ectopic rhythms predispose to myocardial infarction. Gout, xanthomatosis and diabetes mellitus are frequently associated with coronary disease. Other factors include anemia, polycythemia, presence of infection, state of hydration, nutrition and electrolytes, and anxiety, fear, anger and other emotions.

Preoperative medication allays apprehension and helps induction of anesthesia. Mild depressive drugs are useful in older patients as the more potent drugs can cause severe hypotension and respiratory difficulty, resulting in anoxia. Various anesthetic drugs, by their effect on the heart and respiratory mechanism, may cause anoxia, hypercapnia and hypotension which predispose to myocardial infarction during or after surgery. Hypotension is common with spinal anesthesia. The muscle relaxing drugs can cause heart damage by decreasing venous return to the heart, incident to the diminished excursions of the diaphragm and circulatory collapse.

The commonest causes of hypotension during surgery are hemorrhage, reflex effects of visceral manipulation and anesthesia. Hypotension leads to production of thromboembolic phenomena in various portions of the body, particularly coronary occlusion. The following factors during the hypotensive state result in vascular occlusion: reduction of coronary blood flow, stasis and narrowing of blood vessels due to circulating epinephrine and, besides hemorrhage, increased number of blood platelets and reduced antithromboplastic activity of the plasma. The longer the shock, the greater the probability of coronary thrombosis or myocardial infarction without thrombosis.

Tissue injury and subsequent absorption of breakdown products, increase in blood platelets and circulating fibrinogen play a part in postoperative thrombosis. Standard methods of therapy are used for postoperative infarction.

**Pregnancy and Cardiac Operations** Eli J. Igna, Marion F. Detrick, Conrad R. Lam, John W. Keyes and C. Paul Hodgkinson<sup>4</sup> (Henry Ford Hosp.) report data on 22 patients operated on before or during pregnancy. Indications for operation varied. Two nonpregnant patients with patent ductus arteriosus had mild (class II) reduction in cardiac tolerance, recovery from subacute bacterial endarteritis was a determining factor in one. One patient, five months' pregnant when division of patent ductus arteriosus was done, demonstrated no loss in functional cardiac reserve. Three patients with tetralogy of Fallot had cyanosis from birth and severe (class III) limitation of physical activity. In 16 patients with rheumatic mitral stenosis, actual or threatening severe deterioration of cardiac reserve was the precipitating indication for commissurotomy. A major break in cardiac compensation during the present, or in a previous, pregnancy led to operation in seven patients. Cardiac decompensation unrelated to pregnancy was the indication in nine.

All three patients who had division of patent ductus arteriosus were converted to class I. A patient operated on during pregnancy is undelivered, the other two uneventfully delivered term infants. The Blalock procedure for tetralogy of Fallot was unsuccessful in one patient, and her subsequent two pregnancies were accompanied by critical de-

(4) *Am J Obst & Gynec.* 71:1024-1034 May 1956

terioration in cardiac reserve Both infants were delivered prematurely The other two patients were improved to class I One aborted spontaneously when 14 weeks pregnant the other delivered uneventfully a term infant following a normal pregnancy

Commissurotomy for rheumatic mitral stenosis was performed during pregnancy in 5 patients and before in 11 Those operated on during pregnancy were upgraded to class I and remained so during gestation and delivery Two are undelivered One delivered prematurely after spontaneous rupture of the membranes at seven months gestation and two delivered normal term infants Pregnancy followed commissurotomy in nine patients Two received no surgical benefit, and hysterectomy was done during the second trimester Another improved partially from operation but had progressive cardiac deterioration during pregnancy She delivered at term while under strict medical management A fourth patient had deterioration in cardiac reserve and continued her pregnancy to term while on a strict medical regimen Of seven others, all class I patients, two are undelivered two aborted spontaneously at 3½ months, one delivered prematurely when seven months pregnant and two delivered term infants

This experience demonstrated that for all three groups the potential gestational cardiac reserve was most accurately indicated from the degree of improvement resulting from operation, that a successful operative result usually indicated an excellent pregnancy potential, whereas a lesser result was associated with cardiac deterioration during pregnancy

---

## THE AORTA AND PERIPHERAL ARTERIES

Conservative Treatment of Arterial Injuries Caused by Firearms Nguyen-Huu and Phan-Ha-Thanh<sup>5</sup> (Hanoi) report results in 43 patients operated on during the Indo-chinese war 1953-54 The lesions included 5 endarterial contusions with thrombosis, 4 arterial fistulas, 4 lateral wounds, 3 complete sections, 11 arteriovenous aneurysms

(5) *Lyon chir* 50:517-525 July 1955

(2 with fistulas of one vessel), 14 false aneurysms or pulsatile hematomas and 3 secondary hemorrhages caused by cicatricial collapse.

Results were good in 35 (80%), better with sutures than with grafts. In nine patients with lateral suture, results were excellent (no circulatory deficiency or vasomotor disturbance and strong distal pulse) in eight and good (distal pulse somewhat weak) in one. In 23 patients who had end-to-end sutures, results were excellent in 13, good in 6, fair (some vasomotor disturbance and absence of distal pulse) in 2 and poor in 2, 1 requiring amputation. Results were good or excellent in five of six with venous autografts and fair in one. In five with arterial homografts, results were good in only two, fair in one and poor in two (one requiring amputation). Arteries involved were interscalene subclavian, 1; primary carotid, 5; axillary, 7 (1 failure); humeral, 7 (1 fair); common femoral, 6 (1 failure requiring amputation); superficial femoral, 12 (1 failure requiring amputation); popliteal, 11 (1 poor result). Incidence of amputation (two cases) was only 4.6%. There were no deaths.

Diagnosis of arterial injury is often difficult and may require exploratory surgery in doubtful cases. Early operation is most important in successful treatment of arterial wounds. In secondary interventions, the artery is obscured by enormous hematoma or dense perivascular sclerosis which makes dissection hazardous and difficult. Wide exposures, separation of muscles rather than transverse section whenever possible and a meticulously dry field are important technical factors in vascular surgery. To achieve hemostasis, major procedures may be required. In this series, anterior thoracotomy in the third interspace to reach the left subclavian intrathoracic artery and two median total sternotomies to expose the brachiocephalic arterial trunk were performed. Temporary clamps which can aggravate hemorrhage or comprise the vascular wall should not be used; operation should be conducted to permit final suture. Injured vessels should be dissected widely, to include a border of healthy tissue. Blalock's mattress suture is preferred, except for small lateral wounds. Type of operation depends essentially on extent of the lesion. End-to-end suture, the preferred procedure, can be done only when the arterial wall is relatively sound and the distance between cut ends

of the artery does not exceed 3-4 cm. When loss of arterial continuity is over 3-4 cm, vascular grafts must be used, the largest was 12 cm, average, 6-8 cm. Autografts were taken from the superficial femoral vein of the uninjured leg. Fresh arterial homografts were taken from apparently healthy subjects who died during operations for war injuries. Preserved graft was used only once, with a satisfactory result.

**Controlled Hypotension during Operation for Coarctation of Aorta.** Ole Secher, Erik Husfeldt and Frederik Therkelsen<sup>6</sup> (Univ. of Copenhagen) report results in 18 patients, resection of the stenosed area was accomplished in 17, one intervention was merely exploratory. The series comprised mainly children and adolescents.

Hypotension was induced by pendiomid,<sup>\*</sup> a relatively short-acting ganglion blocking drug. The initial dose of 50-75 mg (in two children, aged 5 years and 10 months, respectively, it was 20 mg and in one, aged 4, 25 mg) is given intravenously immediately after the patient is placed in the lateral position. This insures a fall of pressure before incision of the highly vascular muscles. The desired degree of hypotension is harder to achieve in children than in adults. The average systolic pressure was about 100-120 mm Hg, lower pressure was registered only during short periods. Supplementary doses of pendiomid,<sup>\*</sup> usually 20-25 mg (low 5-10 mg, high 50 mg), were given as soon as the pressure tended to rise. The number of injections ranged from 4 to 17. Small blood transfusions were given during operation but merely to compensate for blood loss. After anastomosis was established, no more pendiomid<sup>\*</sup> was given, and the amount of the transfusion was increased to raise the blood pressure to about 120 mm Hg. Only one patient required a sympathicomimetic drug to attain this value.

One patient died shortly after operation. Although autopsy did not reveal the cause of death, change of posture incident to transport to the ward may have been contributory. Another patient died after reoperation because of thrombosis, death was in no way related to controlled hypotension.

Postoperative vomiting occurred in only one patient, who also had a short episode of decreased blood pressure and cyanosis which responded rapidly to oxygen. Another pa-

tient, who had a ventricular septal defect in addition to coarctation, had cardiac arrest when the clamps were removed from the aorta. Immediate cardiac massage restored normal rhythm in seven minutes. Postoperative pulmonary atelectasis had to be cleared bronchoscopically. The patient recovered with no further difficulty.

In 14 cases the postoperative course was uneventful and renal function appeared unaffected. The immediate postoperative rise in blood pressure (characteristic after operation for coarctation of the aorta) was somewhat delayed, because the effect of pendiomid\* usually persists for some hours. This initial increase is followed by a return to normal levels within a week or two.

The authors believe that controlled hypotension during operation for coarctation of the aorta facilitates hemostasis and decreases bleeding. More reliable comparison with previous results can be made only when the present series is augmented and includes more adults.

**Severe Hypertension—Study of 100 Patients with Cardiovascular Complications. Follow-up Results of 50 Controls and 50 Patients Subjected to Smithwick's Lumbodorsal Sympathectomy, 1941-46.** Paul D. White<sup>7</sup> (Boston) states that the two groups of patients were practically identical for age, sex and degree of hypertension and all were followed for at least 10 years. Of 50 control patients, who did not have sympathectomy, 48 are dead, 23 died in congestive heart failure, 15 from cerebrovascular accidents, 4 of myocardial infarction and 2 of coronary insufficiency. The mean survival time was 3.7 years, and the mean age at death was 48.7 years. Of the two living patients, one had a cerebrovascular accident.

Of the 50 sympathectomized patients, 25 are dead, 6 dying in congestive heart failure, 9 from cerebrovascular accidents, 3 of myocardial infarction, and 1 each of coronary insufficiency, atrial standstill, arterial thrombosis, leukemia, cancer, uremia and unknown cause. The mean survival time was 6.1 years and the mean age at death 51.4 years. Of the sympathectomized patients still alive, 20 are in good health, most with blood pressures lower than preoperatively, 4 are in only fair health, and 1 is in poor health. The mean duration of life following sympathectomy in the 25 survivors

(7) JAMA 160:1027-1028, Mar. 24, 1956.

was 10.5 years and in all 50 sympathectomized patients, 81 years, with half still alive. Thus the ratio of longevity in the two groups is already 2:1.

The study indicates that lumbodorsal sympathectomy is much more effective than routine measures in prolonging life, improving health and reducing blood pressure.

► [Probably few doctors realize that so good a record of results for this operation can be compiled. See the following two abstracts—Ed.]

**Three to Seven Year Postoperative Evaluation of 76 Patients with Severe Hypertension Treated by Thoracolumbar Sympathectomy** is presented by H. A. Zintel, A. M. Sellers, W. A. Jeffers, J. A. Mackie, J. H. Hafkenschiel and M. A. Lindauer<sup>8</sup> (Univ. of Pennsylvania). Operative mortality was 0.65%, patient mortality 1.3% and over all mortality, including operative, was 30% during the follow-up period. Most patients were middle aged, 16% were 50 or over. Females outnumbered males by 45 to 31 and there were only 4 nonwhite patients. Mortality of males was 49% and of females 18%. Causes of death included stroke in nine, coronary occlusion in four, uremia in four, congestive heart failure in two, suicide in two, and other causes, two.

Of 53 living patients, 55% had an excellent or fair blood pressure response. Although over all mortality in Smithwick groups 4 and 5 averaged 46%, 33% of all patients in these groups had excellent to fair blood pressure response. Although half the patients with resting diastolic pressures of 140 or more (Smithwick group 5) failed to survive, 9 of 11 survivors had satisfactory results.

Renal function as indicated by blood urea nitrogen and phenolsulfonphthalein excretion did not improve but progressive impairment of renal function was infrequent. Some patients who had high diastolic pressures but normal renal function preoperatively had good blood pressure response (53%), although over-all mortality rate was 47%. Conversely, five patients with marked elevation of diastolic pressure associated with diminished renal function had 60% mortality and the two survivors had poor blood pressure responses postoperatively, indicating that the combination of high diastolic pressures and poor renal function suggests a poor prognosis not improved by surgical therapy. Poor

renal function is the most important contraindication to thoracolumbar sympathectomy for hypertension

Seven of eight survivors with congestive heart failure before operation did not require digitalis, salt restriction or mercurial diuretics postoperatively. Of 11 with congestive heart failure preoperatively who died, only 1 died from failure. Of 16 patients with angina pectoris preoperatively, 14 survived and all but 1 were relieved of pain. Seven of eight patients with history of a cerebral vascular accident with complete recovery, preoperatively, survived, the one death was not caused by stroke. Only half of eight patients who had residual neurologic signs from preoperative cerebral vascular accident survived and three of the deaths resulted from postoperative stroke.

Following operation, postural hypotension, if present, usually disappears within four months. Six patients maintained a postural fall of 20 mm Hg mean arterial blood pressure an average of 62 months after operation. Five of these had an excellent to fair result. Ten patients received antihypertensive or hypotensive drugs because of inadequate postsurgical responses, and seven had an excellent or fair result. This supports the theory that drug therapy is more effective in lowering pressure after thoracolumbar sympathectomy. Before operation, 44 of 53 survivors complained of headache, after operation, only 3.

Survival rates in this series, including operative mortality, are slightly better than those reported by Smithwick in each Smithwick group. The data indicate that thoracolumbar sympathectomy does extend life beyond the expectation in nonoperative therapy.

**Life Expectancy of Surgically and Conservatively Treated Hypertensive Patients** K. H. Pfeffer, H. Nieth and H. Schneider<sup>9</sup> (Univ. of Marburg) compared five year survivals among 206 hypertensive patients with sympathectomy with those among 306 conservatively treated patients. In evaluation of results, patients were classified into two large groups, according to severity of hypertension. Results were especially favorable after sympathectomy in patients with early malignant hypertension. Of 39 patients operated on in this group, 92% survived five years or more, whereas

(9) Deutsche med. Wchnschr. 80:956-958, June 24, 1955



of 56 treated medically, only about 57% survived. Similar results were obtained in those with more advanced malignant hypertension. Of 67 patients with operation, 34.3% survived, whereas only 17% of 65 treated conservatively lived five years. There was no significant increase in survival time of sympathectomized patients with late hypertension. Those with advanced sclerosis of the vessels were not improved by sympathectomy, but uremia as the cause of death decreased significantly.

From the standpoint of survival, best results of sympathectomy are obtained in patients with early signs of malignant hypertension, i.e., increasing blood pressure, progression of eyeground findings and pressure symptoms. In the future, more operations should be carried out in this group. Because of the high surgical mortality from uremia (even though uremia evidently is reduced in those who survive), indications for operation in hypertensive patients with beginning or advanced renal insufficiency should not be extended.

**Chemical Modification of Arterial Homografts.** Gilbert G. Eade, T. Lloyd Fletcher, Ralph J. Schlosser, Ralph K. Zech and Henry N. Harkins<sup>1</sup> (Univ. of Washington) studied the possibility of modifying homografts with chemical agents in an effort to reduce in vivo degeneration. The agents used were ethylene imine, ethylene carbonate, ethylene oxide and propylene oxide. The grafts (72) were treated in the chemicals for 5-180 minutes and stored 1-150 days before being implanted into the thoracic aorta of growing pigs. Storage was carried out at room temperature or at -20 C. with the graft in the agent, in its vapor after the agent was decanted or in alcohol.

That the chemicals appeared to alter tissue composition was suggested by extraction of lipid material during treatment, increased nitrogen content in grafts treated with ethylene imine, analyzed after thorough removal of the agent, and the differences in graft properties following preservation and again after implantation. The treatment was sufficient to prevent growth in tissue culture medium and the grafts were presumed to be dead.

The animals were slaughtered after six to eight months and the in vivo properties of the graft studied, including

(1) *Surgery* 39:515-539, March, 1956.

thelialization and microscopic changes. The ethylene carbonate-treated grafts had good results whether stored at room temperature or at  $-20^{\circ}\text{C}$ . All grafts treated with ethylene imine were severely calcified and lacked dimensional changes. With the other agents the best results were obtained with initial treatment periods of one-half hour or less followed by storage at  $-20^{\circ}\text{C}$ .

The group of chemically treated grafts yielded somewhat better results under certain circumstances than were previously obtained with either fresh or preserved homografts. Dimensional changes, expressed as the percentage of the ratio of graft size increase to host size increase, indicated that the chemical treatment permitted the homograft to enlarge more. The good results were based primarily on the greater ability of the grafts to keep pace with the growing host aorta and the lower incidence of calcification. The histologic differences in homograft behavior were of degree rather than type. Grafts having good results were similar microscopically whether fresh, preserved or chemically treated.

Re-endothelialization was complete except where there was erosion over underlying plaques. Subendothelial proliferation, uniformly present, was greatest over the anastomoses. The internal elastic membrane was usually identifiable. The media was thinned and represented by condensed elastic fibers seen in every stage of degeneration. In no instance were elastic fibers shown to cross an anastomosis. Calcification was usually present. Bone and cartilage were found occasionally in all groups. Elasticity was almost completely lost in all grafts. Fibroblastic proliferation was most evident in segments having the most normal-appearing elastic fibers and the least calcification. Grafts with the greatest dimensional change had the most complete connective tissue replacement, usually the most normal-appearing elastic fibers and the least calcification.

The study shows that if calcification can be delayed and the elastic fibers preserved long enough the host can more completely replace the homograft and transform it into a viable functional structure. Such a unit can undergo physiologic stretching in response to increasing load and thereby

keep pace with the growing aorta in a growing animal Ethylene carbonate is easy to use and alters homografts favorably to provide satisfactory preservation Controlled chemical treatment of homografts may offer a predictable method of graft modification and a possible solution to the problem of homograft degeneration

► {Excellent idea Other substances in the future will probably be found to be superior to ethylene carbonate—Ed }

**Chemically Treated Nylon Tubes as Arterial Grafts** were used successfully in experiments on dogs and in one clinical case by W Sterling Edwards and James S Tapp<sup>2</sup> (Birmingham, Ala )

**METHOD**—The size of a tube of braided Nylon yarn (210 denier) was adjusted to fit snugly over a 5/16 in mandrel giving a finished tube of 1/4 in (0.65 cm) internal diameter

the abdominal aorta of dogs weighing placements include (a) cylindrical tubes, ease of suturing, (b) chemically treated tubes, with physical form conferring a "no kink" feature, and (c) either of above types with conventional textile silicone treatment to decrease angle of contact between blood and pores of tube The Nylon tube on a glass mandrel was immersed for 20 seconds in solution containing 125 parts by volume of 98% formic acid and 45 parts water at 75.85 F and then washed in flowing tap water for 30 minutes For a straight artery, tube and mandrel are left in an air convection oven at 130 C for 30 minutes For a crimped or "no kink" artery one end of tube on the mandrel is pushed toward the other end, causing the tube to assume a circular crimped position while in the oven for 30 minutes

With either type tube is removed from the oven and cooled 30 minutes It is then pushed not pulled off its mandrel and boiled in distilled water for at least 15 minutes this allows crimped tubes to relax slowly and uniformly The tube can be dried overnight in air or can be placed in a 130 C oven for 10 minutes For textile silicone treatment 15 cc of a mixture of five parts Dow Corning Decetex 104 and one part (by weight) Dow Corning XEY 16 is added to 300 cc water Tubes are immersed in this liquid at 75.85 F for 10 minutes then allowed to drain 15 minutes and cured in an air oven at 150 C for 12 minutes Resulting cylindrical tubes were firm but resilient and maintained their shape but flexion of only a few degrees led to kinking and occlusion (Fig 60) The crimped tube could be flexed 180 degrees without occlusive kinking (Fig 61) Both tubes could be cut at any desired level and would firmly hold an arterial stitch 1 or 2 mm from cut edge without fraying

In experiments on 41 dogs anastomosis was carried out with a continuous over and over suture of 5/0 arterial silk interrupted twice After completion of anastomosis with crimped tube the crimps were flattened and compressed with the fingers to straighten the graft In early experiments bleeding was often troublesome corrected by

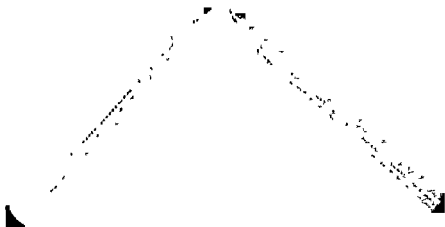


Fig. 60 (top).—Cylindrical braided tubes of Nylon after formic acid treatment, showing inability to kink without kinking.

Fig. 61 (bottom).—Crimped tubes of Nylon showing acute flexion without kinking.

(Courtesy of Edwards, W. S., and Tapp, J. S. *Surgery* 38:61-70, July, 1955.)

wrapping strips of Nylon cloth twice around each anastomosis before release of clamps and holding them in place with a single suture (Fig. 62).

Early gross and microscopic appearance of these chemically treated Nylon tubes shows interstices of the fabric

rapidly filled with fibrin and blood cells. For the first two or three weeks, the inner lining membrane of fibrin can be easily scraped off, and later it becomes firmly adherent and microscopically infiltrated with fibroblasts, which penetrate through the fabric. Grossly, this inner lining membrane begins to take on a polished, gray appearance in the third month. Slight irregularity of inner surface of crimped tubes is further leveled out by production of a thicker lining layer

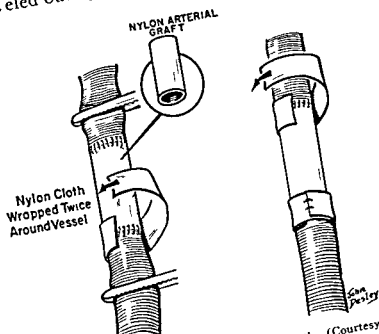


Fig 62—Reinforcement of anastomoses with Nylon cloth (Courtesy of Edwards W S and Tapp J S Surgery 38 61 70 July 1955)

in its concavities. A braided Nylon bifurcation, chemically stiffened for ease of insertion, is now being tested. Successful Management of Obstructive Femoral Arteriosclerosis by Endarterectomy. Experience with Semiclosed Technic in Selected Cases reported by Jack A. Cannon and Wiley F. Barker<sup>3</sup> (Los Angeles) appears to be at least as favorable as that reported by others using homografts. Direct surgical approach can be expected to be beneficial only when the obstructed vessel is large enough to be handled technically and distally joins a patent arterial tree. Restoration of at least one pedal pulse and complete relief of intermittent claudication was obtained in 20 of 23 patients with the popliteal tree patent before endarterectomy

(3) Surgery 38 48-60 July 1955

One patient was considerably improved, but no pulse was obtained: two were not benefited. Of 14 patients with occlusion of the distal popliteal tree, who required surgery because of signs and symptoms of severe ischemia, 1 showed complete relief, 4 were improved and 9 showed no definite change after endarterectomy. No thrombosis occurred in the endarterectomized segment of an artery in which a pulse was restored. Maximal follow-up was 35 months. One of the 14 patients with an unfavorable distal tree died of hemorrhage after rupture of the distal superficial femoral artery caused by a wound infection.

**TECHNIC.**—Preliminary incision is made on the medial aspect of the thigh. The upper portion of the popliteal space is opened and the junction between the superficial femoral artery and the popliteal identified. The artery is explored for collapsibility and adequate backflow. Usually a popliteal arteriogram is obtained. If the popliteal artery is patent and continuous with at least one major branch vessel, the longitudinal incision in the upper end of the popliteal artery is extended about 3 cm. A fine polyethylene catheter is inserted into the distal artery.

Heparin, 10 mg. in 100 cc., is injected into the distal arterial tree at frequent intervals during the rest of the operation. The cleavage plane is then properly started between the thickened intima and surrounding media. A slanting incision is used so that the thickening in the intima is beveled. If necessary, the distal end of the cut edge of the intima is carefully tacked to the arterial wall with interrupted 5-0 silk. The proximal end of the intima, which has been dissected free, is then threaded inside the loop of a fine-wire stripper, and with gentle rotating thrusting motion, the cleavage plane is gradually developed up the artery as far as the stripper will pass without undue pressure. The stripper may pass the entire length of the superficial femoral artery and be exposed at the upper thigh; then the upper end of the intima is approached through an arteriotomy just above the bifurcation of the common femoral artery. Removal of the entire obstructing intima is then possible.

If serious obstruction is found, the artery is exposed at the site of obstruction and an arteriotomy performed under direct vision. After removal of the occluding intima and debris, a rubber French catheter is threaded into the entire length of artery, beginning at the upper end. The lower arteriotomy is closed over the catheter used as a stent, and flushing of catheter and artery with heparin is begun while the arteriotomy is being closed. Heparin is also given intravenously, 25-50 mg. The upper arteriotomy is closed similarly and the catheter removed, with flushing of heparin. Finally, the last segment of the femoral arteriotomy is closed. Clamps on popliteal, deep femoral and common femoral arteries are released in that order. Heparin is continued postoperatively for a few hours to several days, depending on time of return of palpable pedal pulses. The patient is

encouraged to move the leg freely, but ambulation usually is not permitted until the fifth postoperative day.

**Cross-Turned Autogenous Arterial Grafts: Two Years' Observations in dogs** are reported by A Muren, O Dahlback, Ph Sandblom, H Idbohrn and G Norden<sup>4</sup> (Univ of Lund) The method of creating wide autogenous arterial grafts from narrow vessels consists of cross-turning an ar-

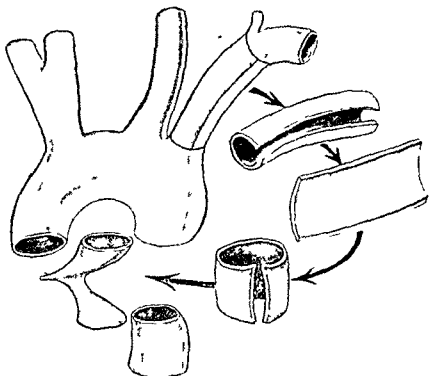


Fig 63—Possible clinical application of method described Cross turned segment of left subclavian artery bridging gap of resected part of coarctated aorta (Courtesy of Muren, A, *et al* Acta chir scandinav 110 403-408 1956)

terial segment, splitting it lengthwise and stitching the short sides together (Fig 63)

**METHOD**—The lower part of the aorta with branches is dissected free and from the left iliac artery a segment, corresponding in length to the circumference of the lower part of the aorta, is resected between ligatures The segment is split lengthwise and the short sides of this rectangular panel are stitched together with continuous sutures to form a cylindrical ring with the same diameter as the aorta After the aorta is cut between Pott's clamps, the preformed arterial ring is sewed in to bridge the gap in the aorta After bleeding has stopped, the graft area is covered with peritoneum and the abdomen closed

(4) Acta chir scandinav 110 403-408, 1956

Observations in dogs after 2, 4, 6, 8, 10 and 12 months' survival were previously reported. Functional and anatomic results were excellent except in one case with thrombus formation at 4 months. In four dogs sacrificed after 24-26 months, aortography showed slight constriction in two, slight dilation in one and marked constriction and uneven contour in one. Elasticity of the graft was about half that of adjoining aorta. When subjected to excess water pressure, the grafts increased an average of about 10% in circumference, whereas the adjoining aorta increased about 20%. Postmortem examination of the intima showed it to be smooth, with no grossly demonstrable thrombotic plaques in three. In two, the graft could hardly be distinguished from adjoining aorta. In one (in which aortogram showed marked constriction) the intima was uneven, with valvelike ridges at the suture lines, presumably because of early thrombosis. Microscopic examinations showed original collagenous layers elastic and muscle cells intact. The only part of the graft that seemed to have been substituted by new tissue was the intima, which was replaced by a rather thick, fibrous layer covered with a thin endothelial lining. In the dog that showed ridgelike projections into the lumen, fibrous tissue was thicker and more vascularized and sutures were surrounded by plasma cells and histiocytes, i.e., more inflammatory reaction than in the others, in which only a scanty lymphocytic infiltration was found.

Functionally, all four dogs remained well throughout the postoperative period. Pulsations of right femoral artery were normal throughout. Left femoral pulsations were not palpable during the first weeks after operation but during subsequent months they reappeared and increased in strength to normal. All dogs gained weight during the observation period.

► [This ingenious method is an important contribution. It is gratifying that the two year results turned out so well.—Ed.]

**Four Year Studies Concerning Fate of Experimental Vena Cava Autografts Used to Bridge Aortic Defects** in 9 dogs are reported by Robert A. Nabatoff, Arthur S. W. Touroff and Milton Gross<sup>5</sup> (Mount Sinai Hosp., New York). Aortography was performed before sacrifice at the following intervals: one at 1 week, two at 1 month, one at 1 year.



two at 16 months, and one each at 2 years, 3 years and 4 years. In routine postmortem studies, gross and microscopic features of the grafts and changes in elasticity were recorded.

All animals remained well and the grafts remained patent. There were prominent pulsations over the area of the graft. Femoral pulses remained palpable and hind limb function was not disturbed. Aortograms performed 15 months or



Fig. 64—Aortogram taken four years following implantation of vena cava graft into abdominal aorta. Note marked ballooning of graft (Courtesy of Nabatoff, R. A., *et al* Surg, Gynec. & Obst 101 20 24, July, 1955)

more following operation revealed dilatation of the graft, which was marked at two years (Fig. 64). Although ballooning persisted, no grafts ruptured. Autopsies confirmed aortographic findings. At 15 months, there was obvious dilatation; grafts appeared to shrink in length as they increased in diameter. At the end of two years, the graft was noticeably shortened and greatly dilated, and with time, the graft wall became progressively thinner.

Microscopic sections showed gradual disappearance of elastic and muscle tissue coats in the vena cava graft. At

15 months, only a small amount of muscle and elastic tissue could be identified. All grafts were surrounded by fibrous tissue elaborated by adjacent host tissues. At the end of four years, the graft consisted essentially of a thin, fibrous tissue tube lined with endothelium.

If a vein graft is used to replace segments of a large artery, it would seem advisable to buttress it externally so it can withstand high intra-arterial pressure.

Experiences with Replacement of Segments of Diseased Femoral and Popliteal Arteries in 16 cases are reported by Ferdinand F. McAllister<sup>6</sup> (Columbia Univ.). Eight procedures were performed for aneurysm, one of which was ruptured at operation; six were for segmental obliteration and two for combined aneurysms and obliteration. In three, the common femoral artery was replaced as part of a general replacement of aorta and iliac arteries. Autogenous vein grafts were used in five instances, with lengths to 15 cm. A preserved homograft was used in one patient with twin femoral aneurysms, and a plastic cloth tube of Vinyon-N was inserted on the opposite side. In the remaining instances, replacements were made with plastic cloth tubes to 42 cm. in length; in eight they were of Vinyon-N, in one, collandered Dacron and in one, Nylon A. In all but four cases, in which the situation was urgent or obvious, preliminary arteriograms were performed. Delays of three to five seconds were employed in arteriograms in an effort to outline the bed distal to the level of the block.

Aneurysms were resected, except for portions of the sac juxtaposed to the accompanying vein, which were usually left in situ. In segmental occlusions, no effort was made to remove the obliterated segment, but the artery was divided above and below and the substitute artery was laid along the diseased vessel, after anastomosing end-to-end above and below. If good pulses were palpated in the feet following insertion of the new segment, no anticoagulant treatment was used. If oscillometrics and pulsations were questionable, heparin and dicumarol<sup>®</sup> were given postoperatively. When peripheral pulses and oscillometrics remained good following segmental replacement, no effort was made to visualize the area. If patency of the vessel was questionable, repeat arteriograms were made. Follow-up ranged from 1½

(6) *Surgery* 38:964-969, November, 1955.

months to 3 years, the longest after plastic cloth prosthesis was 10 months, in a popliteal artery segment, which functioned with good peripheral pulses

Eleven replacements were completely satisfactory, with good distal pulsations and oscillometrics. An additional case was of questionable patency, although calf and foot pain were relieved. Arteriography was deferred in this case because of recurrent thrombophlebitis and subsequent pulmonary embolism.

Thrombosis occurred in two prostheses because of inadequate run-off in the peripheral bed, i.e., plugging into a blind segment of open vessel. Thrombosis occurred in a third case above the site of replacement, following a hypotensive episode. The most important factor in determining patency of the prosthesis seems to be the capacity of the peripheral bed. Preoperative evaluation of this depends considerably on the arteriogram, and often a blind segment is revealed only after five seconds' delay after injection. Bleeding is not necessarily a sign at operation that the vessel is patent peripherally, since some blind segments communicate with a fairly large collateral vessel. If such a segment is plugged into, thrombosis is inevitable.

In segmental occlusion it seems impossible to predict which cases may proceed with progressive obliteration. Therefore, the earlier the situation is corrected, the smaller the segment required for replacement, the better the peripheral run-off and the more likely the chances of success. It would seem desirable to approach the early and minimal claudicators rather aggressively with a view to determining the presence or absence of a small segmental block which may be favorable for correction.

Evaluation of Synthetic Materials and Fabrics Suitable for Blood Vessel Replacement was made by Ralph A. Deterling, Jr., and Shivaji B. Bhonslay<sup>7</sup> (New York). From a consideration of physicochemical characteristics of Nylon, Vinyon N, Orlon, Dacron, Teflon and Saran, it appeared that Dacron might be the best material, with Orlon and Nylon as close second choices, for specialized fabric construction. A study of 16 fabrics indicated that a taffeta weave was most suitable. Smooth surface contour could be achieved by use of low denier, multifilament yarn and by calendering

(7) Surgery 38:71-91 July 1955

process. A certain degree of porosity was considered desirable, which would permit early ingrowth of fibroblasts but without excessive blood loss at time of implantation. Results in several experimental and clinical series in which synthetic fabrics were used to replace defects of the aorta were quite encouraging. The authors had partial occlusion in one Nylon and one Dacron graft in abdominal aortas among 24 grafts implanted in the aorta of dogs.

In the use of synthetic materials for vascular grafts, it is imperative that fabrics be free from impurities. The prosthesis should be critically fitted to the recipient vessel, both in length and diameter, to prevent folds or wrinkling. The cloth should be sewn with a double row of fine stitches of synthetic thread and a fine needle to exact dimensions. Heat sealing may be insecure, unless reinforced by stitching. Vascular suture technic should be meticulous, with closer sutures than usually employed with aortic homografts. All bleeding should have stopped before completion of the operation. Strict precautions and prophylaxis against infection are essential. Though the fabrics are impervious to pus, infection contributes greatly to thrombosis.

Use of synthetic materials for blood vessel replacement, whether a flat fabric or seamless tubes, has been satisfactory, especially in major arteries. Effort should continue to improve existing materials and technics, especially for use in veins and smaller arteries.

Vascular Substitutes are discussed by Oscar Creech, Jr.<sup>8</sup> in an editorial. Excisional therapy in arterial disorders, which is rapidly increasing in use, has resulted in a demand for vascular transplants far exceeding the supply. Arterial homografts are difficult to obtain and are not widely available. Widespread establishment of blood vessel banks consequently has not occurred. The degenerative changes found in experimental homografts are a distinct disadvantage to their clinical use, according to some vascular surgeons. As a result, a search for suitable arterial substitutes is now being conducted with almost phenomenal intensity.

Soon after the pioneering efforts of Voorhees and Blake-more, Shumacker, and Hufnagel, investigation of prostheses made from various synthetic materials was begun in almost every surgical laboratory. Vinyon-N, Nylon, Orlon, Dacron,

(8) Surgery 38:1132-1133, December, 1955.

alon sponge, silica oxide, polyethylene and methyl methacrylate are among the materials studied. Prostheses have been rigid or flexible, pervious or impervious, seamed or seamless, wettable or nonwettable, and shaped into simple branching tubes. The textiles used are generally obtained from lots manufactured for use in wearing apparel and household goods. In some instances, the prostheses are made by the manufacturer, but more often the surgeon fashions them himself, on a home sewing machine.

In experiments to test these prostheses, the vascular substitute is implanted into the thoracic or abdominal aorta of dogs or pigs. The animals are killed at intervals varying from one month to one year after implantation, and the results, in terms of patency and histologic appearance, are noted. In some instances the material is given a limited clinical trial before a report is made. Occasionally the procedure is reversed and the vascular substitute is first tried clinically and then used in experimental animals.

There are several unfortunate features of this type of investigation. The surgeon has the difficult task of attempting to evaluate materials about which he knows almost nothing, as technical aspects of textiles and plastics are not well covered in medical curriculums. It is extremely difficult to obtain separate lots of material with identical properties, especially if procured from the processor rather than the manufacturer. Thus, the results of one phase of an experiment may not be comparable with another, although materials of the same general construction have been used. Usually, there is little attempt to exchange observations except in formal reports, and significant details are often lacking. Occasionally, the surgeon may obtain from a colleague a small amount of material to try, but its specifications and properties are seldom known to him.

These poorly controlled experiments doubtless have some merit, although at the moment their chief value seems to be the opportunity given surgical residents to become skilled in vascular anastomoses. Meanwhile, development of the real vascular substitute is postponed.

Enlisting the technical knowledge and resources of industry can be the solution to the problem of developing a satisfactory vascular prosthesis. This has already been undertaken by at least two investigators in the field. However,

for greatest effectiveness, such a program should be conducted as a co-operative effort by all surgeons interested in vascular disorders. It seems logical, therefore, for one of the surgical societies to appoint a committee to define the properties of an ideal vascular substitute. This committee should secure the co-operation of the chemical and textile industries in developing a suitable prosthesis. As materials are produced, they should be distributed to the vascular centers for experimental and clinical trial, and in this way each material can be carefully evaluated within a relatively short time.

**Arteriogenesis Induced by Tubes of Plastic Mesh.** L. G. Herrmann and Claude Bollack<sup>9</sup> (Cincinnati) studied histologic sections made at intervals of two days to one year at the junction of the aorta with plastic mesh tubes.



Fig 65 (top) — Adventitial layer of fibrous tissue which has been laid down on plastic mesh tube 30 days after implantation of prosthesis

Fig 66 (bottom) — Enlarged view of wall of newly formed artery, showing smooth, glistening, intima like lining of fibroblasts and thick adventitial layer of fibrous tissue with plastic mesh serving as elastic tissue layer of aorta

(Courtesy of Herrmann, L. G., and Bollack, C. *Surgery* 38 993 998, December 1955)

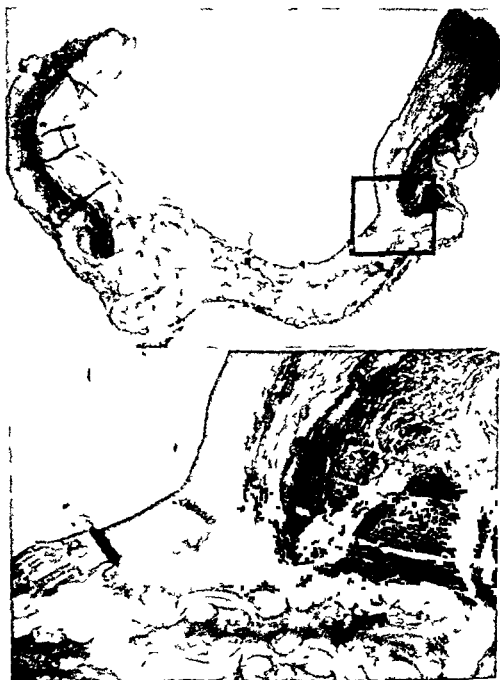


Fig 67 (top) —Cross section of aorta on which patch of nylon mesh had been sewed to repair defect showing degree of autogenesis of layers of artery 97 days later

Fig 68 (bottom) —Enlargement of small square shown in Figure 67 demonstrating that intimal layer of normal artery is continuous with newly formed layer of fibroblasts which forms outside covering of plastic mesh patch

(Courtesy of Herrmann L G and Bollack C Surgery 38 993 998 December 1955)

patches of Orlon or Vinyon-N mesh. It was found that the plastic mesh tube is quickly covered by a layer of fibrous tissue which is continuous with the adventitia of the aorta (Figs 65 and 66). No cellular reaction was evident around fibers of Orlon or Vinyon-N, and only occasional giant cells were seen about the fine silk sutures used to hold the plastic mesh tube in place at the original operation (Figs 67 and 68). The inside lining of the tube was made up of a thin layer of cells of fibroblastic origin, extending through the meshes from the outer layers of the artery and fibrous tissue layer continuous with the adventitia. Within 30 days, a well formed layer of fibroblasts lined the entire plastic mesh tube, and this was continuous with the intimal lining of the aorta above and below the prosthesis. The blood-repellent property of these plastic fibers is probably responsible for absence of thrombosis before proliferation of fibroblasts from outside the tube to the inside is complete.

Bleeding through meshes of cloth of Vinyon-N, mentioned by others, is related to the kind of weave as well as to the physical character of the fiber. Bleeding was not troublesome or serious in the authors' experience. Orlon fiber is smoother and finer and can be woven tighter, consequently, it does not permit as much "bleeding through the mesh." Both Orlon and Vinyon-N mesh are well tolerated by body tissues and possess elasticity closely approximating that of the elastic layer of the aorta. It is believed that seamless tubes of these fibers in various sizes and shapes and with desired branches for renal arteries, common iliac arteries and even smaller arteries, will be fabricated by some ingenious person in the near future.

**Quantitative Observations during Freeze-Dry Processing of Arterial Segments** by three different technics were compared by Sigmund A. Wesolowski, Lester R. Sauvage and Roger D. Pinc<sup>1</sup> (Walter Reed Army Med. Center). Vapor-pressure-time curves for various loads of adult pig abdominal aortas and human aortas were studied with the Cryostatic Doublet diffusion pump, glass manifold and trap system and brass trap manifold system. The Cryostatic Doublet diffusion pump system represents the ultimate in design for freeze-drying of arterial segments, but the manifold systems are easier to operate, less expensive and prac-

(1) J. Thoracic Surg. 30:933, July 1955.



tically as efficient. With loads not exceeding 20 Gm of ice per port, these systems are practical equivalents. An 'overnight run' will reduce water content of arterial segments to 1% or less. If measurement of vapor pressure of the specimen side of the cold vapor trap is not feasible or if doubt exists, a 24 hour processing should suffice. In loading specimens into tubes, jamming arteries into the bottom must be avoided. If there is no space between the wall of the arterial segment and that of the tube, at least along one side, the bottom of the specimen may be melted during processing. It is also advisable for vessels to be processed rounded rather than collapsed.

Drying temperature of average loads (e.g., entire human aorta in three tubes) varies from  $-30$  to  $-35^{\circ}\text{C}$ . Use of a dry ice alcohol mixture ( $-72^{\circ}\text{C}$ ) as the coolant about the vapor trap is as effective as liquid nitrogen ( $-196^{\circ}\text{C}$ ) when processing untreated vessels. However, if ethylene oxide is used to sterilize the arteries, dry ice alcohol is contraindicated as the trap coolant; liquid nitrogen is adequate in these circumstances.

Inclusion of a diffusion pump in the vacuum system shortens the drying cycle but does not significantly affect drying temperature of arterial segments during processing. An adequate mechanical pump alone is sufficient for practical laboratory processing. Processing continued two to four hours after vapor pressure on the specimen side of the cold trap returns to base line level results in arteries with a final moisture content of 1% or less.

It is recommended that specimen tubes containing ethylene oxide treated vessels be kept surrounded by a dry ice alcohol mixture during the first hour or two of processing. At  $-72^{\circ}\text{C}$  treated vessels undergo some drying where untreated vessels exhibit no drying. Treatment of arterial segments with 1% beta propiolactone before freeze drying does not affect vapor pressure time curves during processing.

**Some Practical Considerations in Surgery of Blood Vessel Grafts.** Blood vessel grafts are used in (1) obliterative diseases and (2) aneurysms of the aorta and the major arteries. (3) injuries that have resulted in interruption of the arterial continuity secondary to thrombosis or division of an artery. (4) tumors situated near major arteries in which

it is necessary to resect these blood vessels to perform an adequate cancer operation, and (5) congenital vascular lesions. The types of blood vessel grafts include: (1) autogenous venous, (2) homologous venous, (3) homologous arterial and (4) synthetic fabrics.

According to Robert R. Linton<sup>2</sup> (Massachusetts Gen'l

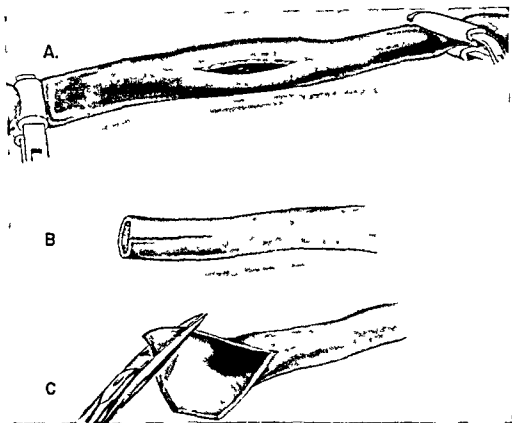


Fig 69—Drawings showing end to side technic of an arterial anastomosis *A*, in a portion of host artery isolated between two bulldog clamps an incision is made about two to three times as long as the diameter of the artery *B*, the graft (venous or arterial) is prepared by making a longitudinal incision from the cleanly divided end, approximately as long as the incision in the host artery *C*, corners of arterial flap are cut away (Courtesy of Linton R R Surgery 38 817 834, November, 1955)

Hosp), autogenous venous grafts have to be stored, are easily available (usually the internal saphenous vein) and cause no antigenic reaction. However, the autogenous venous graft is seldom large enough to be used as an aortic or iliac graft, is not suitable for artery replacement, has valves and is difficult to manipulate. It is best reserved for short arterial grafts in the femoral arteries. The homologous venous graft has the same advantages and disadvantages as the autogenous venous graft plus increased incidence of

(2) Surgery 38 817 834, November, 1955

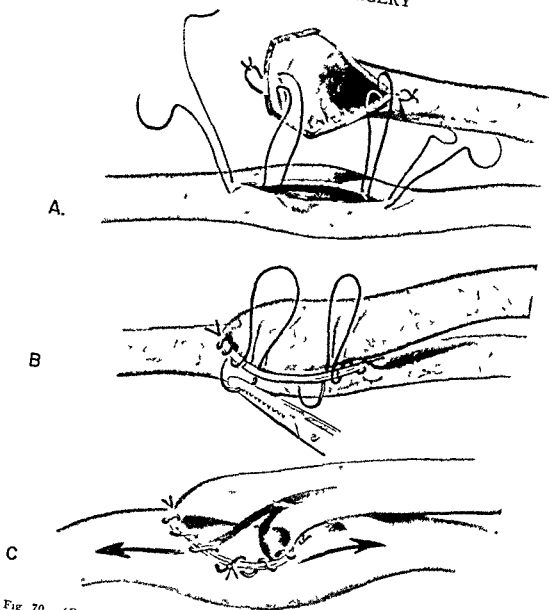


Fig 70—(End to side technic cont) A two mattress sutures with needles at each end of 50 silk are first used to join graft with host artery as shown. The needles are passed through graft wall from outside to inside and on host artery in reverse direction to prevent dislodgment or separation of friable intima of host artery. B mattress sutures are tied then each end is used to complete the anastomosis with a running over and over stitch. The two ends are tied in middle of suture line. Note again that needles always pass from inside to outside of host artery—important in preventing separation and fragmentation of intima. C completed anastomosis. Arrows indicate flow of blood in both directions in host artery. Note also funneling or widening produced in end of graft and at site of anastomosis in host artery—important in reducing incidence of thrombosis at this site (Courtesy of Linton R R Surgery 38 817 834 November 1955)

thrombosis. It is best used for short segments of the iliac, femoral and popliteal arteries. The homologous arterial graft is the most useful and satisfactory for aortic and arterial replacement. Secondary thrombosis is less common

with it than with other types of grafts, and it can be obtained in any size or length. These grafts should be obtained from the limbs of fresh bodies that have been kept refrigerated near 0 C. Synthetic fabrics will some day be the most commonly used graft material.

The methods of preservation of homologous blood vessel grafts include the (1) nutrient broth method, (2) the quick-freeze method, (3) the freeze dry method and (4) the frozen-irradiated method. Grafts preserved by the nutrient broth method must be obtained under sterile conditions and can be stored only for 30-40 days. Grafts preserved by the quick freeze method must be obtained under sterile conditions and stored at low temperatures. The freeze dry method is a satisfactory one because the grafts do not have to be obtained under sterile conditions and can be stored at room temperature. The frozen irradiated method is the most satisfactory because the cathode rays kill all bacteria and tumor cells, and thus almost any body can be used to obtain the grafts. These grafts can be stored for almost indefinite periods.

Arteriography is necessary preoperatively to determine the type and extent of the vascular disease. The requirements of a successful blood vessel graft are: (1) availability of a suitable graft for by passing the obstructed portion of the diseased blood vessel, (2) a site of the proximal anastomosis at a level sufficiently high on the patient's arterial system to supply an adequate inflow of arterial blood through the graft to prevent thrombosis, (3) an adequate arterial bed distal to the distal anastomosis of the graft to permit a satisfactory arterial outflow, (4) preoperative arteriograms, (5) meticulous technic, (6) the use of heparin, (7) meticulous apposition of the surrounding tissues of the host to the graft, and elimination of all dead spaces in which serum and blood might collect, and (8) rigid aseptic precautions.

The causes of graft failure are: (1) poor surgical technic, (2) inadequate arterial system distal to the graft, (3) infection with secondary hemorrhage, (4) leakage and (5) secondary thrombosis.

The types of anastomoses are end to end and end to side. The end-to side is more easily constructed and produces an anastomosing stoma which is wider than the caliber of

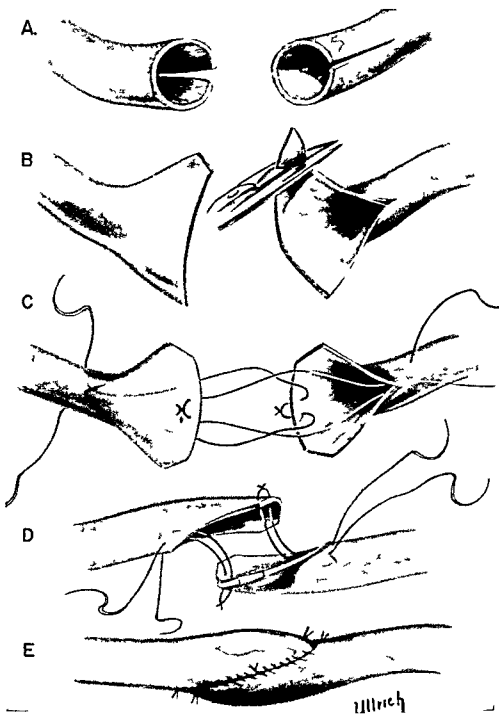


Fig. 71—Drawings showing end-to-end anastomosis by end-to-side technic. *A* cleanly divided ends of grafts are incised longitudinally about two to three times the length of their diameters. *B* corners of square-ended arterial flaps are trimmed. *C* *D* two everting mattress sutures of 5-0 silk are first placed to bring together the middle of each arterial flap of one graft to the acute angle of the longitudinal incision of the other graft. *E* after tying the mattress sutures the ends are used to complete the anastomosis using a running over-and-over stitch which produces excellent intima-to-intima approximation (Courtesy of Lanton R. R. Surgery 38:817, 834 November 1955).

either the graft or the host artery (Figs 69 and 70), so that thrombosis at the site with failure of the graft is less likely to occur than when the end-to-end type of anastomosis is used. The end-to-side method is used for small vessels. The end-to-end method is used for the proximal suture of an aortic graft to the aorta or common iliac limbs of an aortic bifurcation graft to the common iliac arteries of the host or another graft. The technic of end-to-side type of anastomosis has also been used to construct end-to-end anastomoses, especially in suturing two grafts together (Fig 71).

Adequate exposure is essential for vascular surgery. The insertion of an aortic graft necessitates an incision extending from the umbilical process to the pubis. Oblique incisions in the thigh are utilized for the femoral and popliteal arterial grafts. Multiple incision should be used in the lower extremity rather than one long incision. All incisions should be closed without drainage.

**Occlusive Disease of Terminal Aorta** results in characteristic symptoms, known as the Leriche syndrome, which recently has been recognized as being surprisingly common. It affects women as well as men, is often of insidious onset and may produce incapacitation. Its exact pathogenesis is not clear, but pathologic characteristics are relatively constant. Intima and media are thickened to such extent that the vascular lumen becomes exceedingly narrow. Thrombosis develops at these sites and may then cause complete occlusion, most commonly at the aortic bifurcation, usually with involvement of proximal reaches of common iliac arteries. Marked narrowing or occlusion of the terminal aorta prevents normal pulsatile blood flow into iliac vessels and thus into lower extremities through the main arterial channels. Complete occlusion is not necessary for production of symptoms, since severe intermittent claudication may be present in patients with very narrow but patent vessels.

According to John W Kirklin and F Henry Ellis, Jr<sup>3</sup> (Mayo Clinic), diagnosis of occlusion of the terminal aorta can often be made clinically on the basis of intermittent claudication involving the thighs, lateral aspects of hips, buttocks or lumbar regions. This is in contrast with arteriosclerosis obliterans in leg vessels, in which claudication most often begins in the calves. In occlusion of the terminal

aorta, pulses in the arteries of the lower extremities are diminished or absent. Usually signs of ischemia of the feet are minimal or absent. Clinical diagnosis should be confirmed by translumbar aortography, to localize the obstruction exactly and to determine the patency of the aorta or iliac vessels below the occlusion.

Exploration for resection and grafting is advised in all patients with clinical and aortographic evidence of occlusion who have severe symptoms. Age is not ordinarily a contraindication, but severe coronary lesions make operation for benign disease inadvisable. If, at operation, exploration of vessels distal to the main level of occlusion reveals that they are patent, resection and grafting are carried out. If no lumen can be demonstrated by actual sectioning of external iliac vessels and if vessels appear to be solid down to the inguinal ligament, bilateral sympathectomy is performed instead of resection and grafting.

**TECHNIC**—Resection must be carried beyond the distal extent of obstruction. Occlusion is usually limited to the region of the aortic bifurcation and only terminal aorta and upper reaches of common iliac arteries are excised after clamping the aorta above and the iliac arteries distal to the point of obstruction, and appropriate dissection is carried out. As soon as clamps are placed on the iliac vessels, 5 to 10 cc heparin (50 mg/100 cc) is injected distal to the clamps before further dissection to prevent intravascular thrombosis. Arterial continuity is restored with a Y graft of preserved homologous aorta. All anastomoses are made with 5/0 silk with a continuous over and over stitch interrupted at each angle. Before the distal anastomoses are made clamps on iliac vessels are released to flush out any small thrombi. After clamps are replaced, heparin solution is again instilled into the iliac vessel, and at completion of the anastomoses the graft is filled with diluted heparin solution. Normal pulsations should be present in the distal vessels after clamps are removed. If not, the anastomosis must be remade so that good flow occurs. After conservative bilateral lumbar sympathectomy, the posterior peritoneal peritoneum is closed over the entire graft. A strong closure of the abdominal wall is essential to prevent postoperative complications.

In 18 patients subjected to this procedure, there were no postoperative deaths and no serious complications. In a few in whom spotty areas of occlusion lay in the external iliac and femoral vessels were suspected at operation, thrombosis occurred either in the suture line or in the graft. Physiologic and functional results following resection and grafting of the terminal aorta, however, are excellent when iliac and femoral vessels are patent distal to the graft. Relief has persisted in some patients followed as long as a year and a half.

## PERIPHERAL VEINS

**Varices, a Sign of Vascular Malformations: Attempt at Classification.** Cl. Olivier<sup>1</sup> (Paris) emphasizes the importance of identifying the vascular malformations responsible for certain classes of varices, i.e., those due (1) to agenesis of the deep venous trunks, (2) to congenital arteriovenous fistula and (3) to angiomas. Arteriography and phlebography are the principal diagnostic methods by which the underlying malformation can be identified, and both prognosis and choice of treatment depend on the information they supply.

Since the subcutaneous venous trunks often constitute the only pathway for return of venous blood in patients with varices due to agenesis of the deep venous trunks, their occlusion merely aggravates the disorder. Occlusion must therefore not be attempted either by sclerosis or by surgery. Varices of this class are often accompanied by verrucous or vascular nevi and hypertrophic lengthening of the affected limb, which are the other members of the triad of changes found in patients with varices due to congenital malformations.

In varices of the second class the arteriovenous communication is direct, without any intervening angiomatous formation. The late prognosis of these arteriovenous fistulas must be reserved; in some patients they may be completely eliminated, but in others they will reappear, either in the same limb or elsewhere in the body. Arteriovenous fistulas are sometimes closely related to the appearance of gravidic varices, but Olivier believes that all that is involved in this case is a temporary opening of the canals of Sucquet under endocrine influences. The disturbance, therefore, is physiopathologic and not anatomic. Congenital arteriovenous fistulas represent a permanent abnormal communication between an artery and a vein. Instead of remaining stationary or showing a tendency toward spontaneous regression, they have a capacity for development that may even make amputation of the affected limb necessary.

Varices due to angiomas must be distinguished from

---

(4) *Presse méd* 63 1822 1825, Dec 25, 1955



those associated with, but not caused by, angioma. Structurally, the subcutaneous lesions caused by angioma occupy a position midway between angiomas and varices and may be called varicose angiomatoses. They may appear either as isolated lesions or in association with deep limited or diffuse angiomas. When isolated, they are sometimes amenable to surgical treatment, careful attention, however, should be given to the patient's age and general condition before the operation is undertaken. When they are associated with deep angiomas with arterial circulation they are generally beyond the reach of surgery. The best treatment in such cases seems to be compression of the varicose segment of the limb by elastic bandages, with it, the functional symptoms at least are relieved.

**Comparative Studies of Blood of Normal and Varicose Veins** are reported by A. Greither<sup>5</sup> (Univ. of Heidelberg).

**METHOD**—After 10-12 hours of complete bed rest, blood was removed simultaneously from cubital veins and from a varicosity of the saphenous vein without application of a tourniquet, while the patient rested in a reclining position. The patient then walked slowly for 1 hour without compressive bandages, climbed stairs and finally stood still for 10-15 minutes. Blood was then taken from normal and varicose veins with the patient erect. Laboratory studies included analysis of globulin and albumin, platelet count, clotting time, CO content, nonprotein nitrogen and oxygen content of blood.

As was expected, there was no recognizable difference in compensated and decompensated cases of varicose veins. Seven males and 18 females were examined, of whom 15 had decompensated varicosities coupled with crural ulcers.

There is no difference between blood composition in varicosities and blood taken from intact veins, either chemically or morphologically. It follows that such sequelae of varicosities as edema, dermatitis, eczema and crural ulcer are hemodynamic and static problems rather than problems of blood chemistry.

**Varicose Veins. Results of Surgical Treatment.** S. W. Moore and William L. Craver<sup>6</sup> (New York Hosp.-Cornell Med. Center) compare 100 cases (170 extremities) treated by high ligation and complete stripping of the great saphenous vein to the region of the medial malleolus, with 312 cases (476 extremities) treated by other operations, principally stripping to the mid-thigh or knee and multiple liga-

(5) *Angiology* 6:533-536, December 1955.

(6) *Ann. Surg.* 143:500-503, April 1956.

tions. Of the 646 extremities, 561 (86.8%) were followed, by re-examination, for one to eight years. Beyond one year there was little change in comparative end results.

There were 247 females (60%) in the series. The right side was operated on 320 times (49.5%), the left side 326 times (50.5%). Age range was wide, but most patients were between 40 and 60 at time of operation. With stripping to the ankle, an average of 4.3 days were spent in the hospital, this compares favorably with other procedures and is notably shorter than hospitalization (5.1 days) after multiple ligation. Over half (54%) the extremities subjected to stripping to the ankle required no postoperative injections, only one third having multiple ligation or stripping to the knee did not require injections. There were no postoperative deaths, and five during the follow up period were not related to the operation or to varicose veins.

Superficial wound infections were the most common complication, three occurred in the group with stripping to the ankle. Three saphenous nerve injuries occurred with multiple ligation and two with stripping to the ankle. There was no pulmonary embolism.

End result of high ligation and stripping to the medial malleolus was excellent in 59% and good in an additional 19%. This is  $2\frac{1}{2}$  times the percentage of excellent results after multiple ligation and over twice that after stripping to the knee. Complete stripping to the ankle also had the lowest percentage (8%) of poor results. These results are comparable to those recently reported from the Mayo Clinic, indicating that the radical stripping method is the procedure of choice.

**Rationale and Results of Popliteal Vein Division.** According to Gunnar Bauer<sup>7</sup> (Mariestad, Sweden) the competence of the femoral vein valves and the pumping action of the calf muscles prevent edema of the lower extremities. This highly efficient auxiliary pumping mechanism acts as a peripheral heart. Diseases of the muscles are extremely rare, but diseases of the valves are common, and are the most common cause of edema and ulcers of the lower extremities. The main cause of femoral valvular insufficiency is post thrombotic valvular incompetence. Of 650 patients with incompetence of the femoral vein valves, 329 had post-

(7) *Angiology* 6:169-189 June 1955

ombotic and 321 idiopathic incompetence. Retrograde phlebographic studies demonstrated the mechanism of femoral vein incompetence in preventing edema of the lower extremities.

If femoral vein incompetence exists, permanent blocking of the incompetent vein trunk at its lower end, the popliteal vein, will prevent stasis and edema in the lower extremity. If the popliteal vein is blocked, other collateral pathways existing past the level of the knee joint upward to the femoral vein will take over the circulation. Phlebographic studies have demonstrated these pathways.

Treatment consisting of double ligation of the popliteal vein and resection of the intermediate segment was given to 650 patients. All accessory popliteal veins were also resected. Ligation and sclerosing of incompetent superficial veins were done in 15%. All patients had supportive bandaging for at least four months. A continuous follow up for three years after operation was made in 350 patients with severe cases, all of whom had had marked edema with associated ulceration for eight to nine years. In 75.7% of the patients the leg remained healed and the patients were entirely asymptomatic. In 24.3% the edema and ulceration recurred once or oftener. The recurrences took place in the first postoperative year in about 75% and in the second year in all but two patients. A similar continuous follow up study, covering a period of six years, was made in 100 patients. In 74% the leg remained healed, and in 26% recurrences occurred. Of the recurrences 19 occurred in the first postoperative year, 4 in the second, 1 in the third, 1 in the fourth and 1 in the sixth. The study showed that popliteal vein division is both theoretically and empirically satisfactory.

**Thrombophlebitis of Superficial Veins of Breast and Anterior Chest Wall (Mondor's Disease)** in 43 cases (1 in a man) is reported by Joseph H. Farrow<sup>8</sup> (Memorial Center for Cancer, New York). Only 58 cases have been reported in the literature, but the condition must be more common than generally recognized as the present series was seen in an eight year period, 18 in the last year of that time.

Thrombophlebitis occurred following mild trauma in 4 instances, skin ulcer in 1 and postoperatively in 14. Etiology

8) Surg. Gynec. & Obst. 101:63-68, July 1955.

was not determined in 24, although large and pendulous breasts in middle-aged women seemed particularly prone to spontaneous appearance of this condition. There was no apparent relationship to benign or malignant breast lesions.

Principal symptoms are localized tenderness and pain but these are relatively mild. The thrombophlebitic vessel appears as a slightly tender and firm subcutaneous cordlike structure attached to the overlying skin. Elevation of the breast or stretching the skin produces a deformity characterized either by a shallow groove or a narrow ridge (Fig. 72).

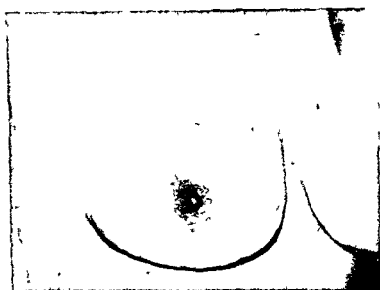


Fig 72—Patient, 50 with arm elevated, showing branching of subcutaneous cord, skin retraction and deformity similar to that seen in mammary cancer. No mass palpable in breast. Follow up examination a year later revealed no cancer. (Courtesy of Farrow, J. H. Surg., Gynec. & Obst. 101:63-68, July, 1955.)

On the basis of skin retraction and an indurated subcutaneous cord the infrequent but serious erroneous diagnosis of lymphatic permeation from occult breast cancer is sometimes made.

Biopsies can be done in doubtful cases, but usually physical findings are sufficiently diagnostic. Treatment is rarely required, since thrombophlebitis subsides spontaneously, with disappearance of deformity and palpable cordlike structure in six weeks to two months. In one patient an asymptomatic web on the inferior surface of the breast persisted 10 months. None of the 43 patients had recurrence of thrombophlebitis locally or in other areas.

**Pectoralis Minor Tenotomy and Anterior Scalenotomy with Special Reference to Hyperabduction Syndrome and "Effort Thrombosis" of Subclavian Vein.** The subclavian artery and vein may be stretched and acutely angulated as they pass beneath the pectoralis minor tendon in the position of hyperabduction. Jere W. Lord, Jr., and Peter W. Stone<sup>9</sup> (New York Univ.) report on five patients with hyperabduction syndrome, refractory to conservative measures, who had section of the pectoralis minor tendon and division of the anterior scalene muscle through a separate incision.

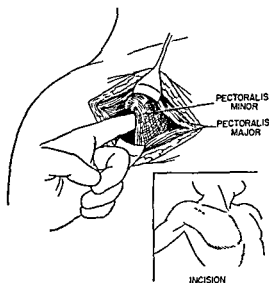


Fig 73—Pectoralis major muscle divided in direction of its fibers. Finger of the operator is behind tendon of pectoralis minor muscle. Inset shows approximate position and direction of skin incision for pectoralis minor tenotomy. (Courtesy of Lord, J W, Jr, and Stone P W. *Circulation* 13:537-542, April, 1956.)

**TECHNIC**—A 3 in oblique incision is made just below the coracoid process and is deepened to the pectoralis major muscle which is incised and split in the direction of its fibers. The tendon is divided about  $\frac{1}{2}$  in from its point of insertion (Fig. 73). The 3 in transverse incision for anterior scalenotomy is made  $\frac{1}{2}$  inch above the medial end of the clavicle and is extended through the platysma muscle. The clavicular attachment of the sternocleidomastoid muscle is divided if it cannot be adequately retracted. The phrenic nerve is mobilized from the anterior surface of the scalenus anticus, which is then divided about 1 cm from its attachment to the first rib. If marked narrowing of the space between the clavicle and first rib is associated with a clinically positive costoclavicular maneuver, total claviclectomy is performed, with removal of the periosteum. Otherwise, the clavicular head of the divided sternocleidomastoid muscle is repaired with interrupted sutures of silk or cotton.

(9) *Circulation* 13:537-542, April, 1956.



necessary to exercise meticulous laboratory control, with careful regulation of dosage

Marcumar represents a significant advance over dicumarol® and has undoubtedly brought the day of general prophylaxis nearer. However, postoperative hemorrhage induced by marcumar should not be tolerated for the sake of prophylaxis against thrombosis. Therefore, patients are carefully studied from the standpoint of liver function. Dosage is determined individually under strict laboratory control. With increased coagulation, especially a lower value on the Quick test, marcumar is abandoned as readily as dosage is increased when the Quick test result is high.

Ideal prophylactic therapy has not yet been achieved. There is need for an effective drug that is even better and more consistently tolerated than marcumar, and that might be administered to all surgical patients. There is also need for a better method of recognizing the danger of thromboembolism earlier, which would allow better planning of therapy.

---

## LYMPHATIC SYSTEM

Chronic Edema due to lymphatic block and that due to venous obstruction used to be differentiated, but, according to Ian Aird<sup>2</sup> (Postgrad Med School London), this distinction is no longer valid. Both should be referred to as "chronic lymphedema," to distinguish them from chronic edema due to heart or kidney disease which does not become solid.

In chronic lymphedema of any kind, fluid first collects in subcutaneous tissues. Later, lymphocytes and even lymph follicles can be detected in the fluid spaces. Soon a network of fibrin is laid down first in deeper layers, but later in the whole thickness of subcutaneous tissue. Still later fibroblasts appear first in deeper parts of the subcutaneous space, on the surface of the deep fascia, but later increasing in depth toward the skin until the whole subcutaneous tissue is replaced by a dense fibrous mass. At this stage pitting is lost, and edema becomes solid. When replacement of subcutaneous tissue by fibrosis and clotted lymph is complete, the

skin thickens also, becomes discolored and in places proceeds to frank ulceration. If careful search is made for the cause of edema, relatively few cases remain in the category of spontaneous lymphedema or lymphedema praecox.

There are six congenital causes of chronic edematous thickening of subcutaneous tissues: (1) Milroy's disease or lymphatic fibrous hypertrophy, which is strictly congenital and inherited, (2) congenital arteriovenous fistula, which gives rise to a true chronic edema manifest as a rule only in adult life, (3) congenital lipoedema, which is not a pure edema, its main feature being a localized deposit of fat in subcutaneous tissues of the lower limbs and buttocks, (4) diffuse lymphangiomas in the subcutaneous tissues of the limb may be associated with slight edema of the distal part of that limb, though the chief complaint is usually of localized swelling produced by the lymphangioma, (5) congenital neurofibromatosis may be associated with some very solid edema, and (6) so called amniotic bands may produce a chronic edema distal to the constriction, or this may be present at birth.

Other types of lymphedema include allergic, inflammatory, post-traumatic, postoperative, that due to erythrocytosis frigida, thrombophlebitic, parasitic, caused by blockage of lymphatics by filaria (*Wuchereria bancrofti* or *malayi*), artefacta (sometimes self-induced by application of a constricting band) and neoplastic. When all possible causes of chronic edema have been excluded, there remain numerous patients with "spontaneous lymphedema" in whom no cause can be found. Usual onset is soon after puberty, with spontaneous swelling in foot or ankle, usually on one side at first, gradually extending up the leg over months and years but rarely spreading to the abdomen or flank. In rare cases of lymphedema of the legs, the skin of the thigh and lower abdomen may present vesicles filled with milky chyle. This type chronic edema can be cured by ligation of the chyle filled lymphatic trunks in the thigh or pelvis.

Treatment of lymphedema is quite disappointing. Inflammatory and allergic varieties may benefit from frequent massage of the affected part under penicillin cover, and temporary relief may be obtained with antihistamines. Fluid or pitting edemas may be reduced by cortisone or ACTH, but



when these drugs are stopped, swelling returns within a few hours. All pitting forms can be reduced by bed rest, elevation and massage, followed by elastic bandaging. It is more difficult to rid an arm of edema than a leg. Sympathectomy has not been successful except in some cases of thrombophlebitic type in which the lower extremity is palpably cold. Effect of sympathectomy can be predicted by alcohol block. Ligation of the femoral and of superficial communicating veins is usually unsatisfactory in thrombophlebitic cases. Fungous infection in the toes should always be brought under control.

In solid edemas, surgery is required. The most satisfactory operation is excising the subcutaneous tissue and covering with a skin graft. In some instances, hinged flaps can be used, but if the skin is widely ulcerated or thickly fibrous, it is removed completely, with the deep fascia, and free grafts are applied directly to the muscle. In extreme and painful degrees of solid lymphedema with recurrent inflammation and ulceration, amputation may be the kindest treatment, but when both limbs are affected, its benefit is disputable. In patients in whom amputation of the edematous portion has been performed, the normal subcutaneous tissues of the stump, above the previously diseased level, quite often subsequently proceed to edema.

Treatment of Lymphedema depends on complete co operation between physician and patient in applying physiologic and psychologic principles over long periods, according to William T. Foley<sup>3</sup> (New York Hosp. Cornell Med. Center). He reports six cases of postmastectomy edema of the arm and five of lymphedema of the leg studied for two to seven years. All patients received physiologic treatment, consisting of nightly elevation, daily compression and massage, until edema had been reduced to a minimum. An effort was then made to evaluate treatment with hyaluronidase and implanted nonabsorbable sutures. Hyaluronidase in doses as high as 1,500 turbidity reducing units, repeatedly injected, did not reduce edema further. Long, nonabsorbable sutures, buried in subcutaneous tissue and extending from the edematous region to normal areas, also had no effect.

Gravity, compression, massage and dehydration (low salt diet and daily injection of 1-2 cc. thiomerin® during the first

(3) Surg. Gynec. & Obst. 101:25-34, July 1955.

week of hospitalization) are of great value in reducing post-mastectomy edema of the arms and lymphedema praecox of the legs, and in maintaining improvement during years of supervision. Patients are encouraged to resume full activity and sports, wearing an elastic stocking or sleeve, to promote the pumping action of muscular movement on venous return and lymph flow.

► (It is curious that no operative procedure is mentioned especially for treatment of lymphedema of the legs & modified Kondoleon operation or the procedure described by Aird in the preceding abstract will sometimes be rewarding—J d.)

### Abnormalities of Human Superficial Cutaneous Lymphatics Associated with Stasis Ulcers, Lymphedema, Scars and Cutaneous Autografts were studied by Harvey R. Butcher, Jr. and Alice L. Hoover<sup>1</sup> (Washington Univ.)

**METHOD**—The method of Hudrick and McVisters slightly modified was used for studying the pattern of the superficial cutaneous lymphatics. A tunnel was made into the upper layer of dermis with a 30 gauge hypodermic needle. Into this tunnel 0.02 ml. of 4% sky blue dye was injected through another 30 gauge needle attached to a tuberculin syringe. Slight pressure on the plunger and lateral motion of the needle facilitated the entrance of dye into the dermal lymphatics. Photographs were taken 30, 60 seconds after injection using a Wratten A filter in aperture of f32 in exposure of 1/1000 second and speed flash illumination.

The patterns of the superficial dermal lymphatics outlined in the skin of the extremities of normal persons showed little variation in length, diameter and number of lymphatics in the dermal reticular network. The appearance of the reticular pattern was consistent and reproducible.

Superficial cutaneous lymphatics were usually absent in the skin about stasis ulcers and over "hard" lymphedema (Fig. 74). They were dilated overlying "soft" lymphedema and were normal over simple varicosities and with cardiac and nutritional edemas. They were initially dilated in split thickness autografts and soon established communications with lymphatics in contiguous skin. Endurance of lymphatics in a graft appears requisite for its continued survival. Dermal lymphatics establish connections across incisions by the 12th to 14th postoperative day, with healing per primam. They were found to be few in number, and of small caliber in old dense scars of the skin after healing per secundum. The superficial lymphatics can be obliterated by sterile

(4) Ann Surg 142:633-653, October 1955

when these drugs are stopped, swelling returns within a few hours. All pitting forms can be reduced by bed rest, elevation and massage, followed by elastic bandaging. It is more difficult to rid an arm of edema than a leg. Sympathectomy has not been successful except in some cases of thrombophlebitic type in which the lower extremity is palpably cold. Effect of sympathectomy can be predicted by alcohol block. Ligation of the femoral and of superficial communicating veins is usually unsatisfactory in thrombophlebitic cases. Fungous infection in the toes should always be brought under control.

In solid edemas, surgery is required. The most satisfactory operation is excising the subcutaneous tissue and covering with a skin graft. In some instances, hinged flaps can be used, but if the skin is widely ulcerated or thickly fibrous, it is removed completely, with the deep fascia, and free grafts are applied directly to the muscle. In extreme and painful degrees of solid lymphedema with recurrent inflammation and ulceration, amputation may be the kindest treatment, but when both limbs are affected, its benefit is disputable. In patients in whom amputation of the edematous portion has been performed, the normal subcutaneous tissues of the stump, above the previously diseased level, quite often subsequently proceed to edema.

Treatment of Lymphedema depends on complete co-operation between physician and patient in applying physiologic and psychologic principles over long periods, according to William T. Foley<sup>3</sup> (New York Hosp.-Cornell Med Center). He reports six cases of postmastectomy edema of the arm and five of lymphedema of the leg studied for two to seven years. All patients received physiologic treatment, consisting of nightly elevation, daily compression and massage, until edema had been reduced to a minimum. An effort was then made to evaluate treatment with hyaluronidase and implanted nonabsorbable sutures. Hyaluronidase in doses as high as 1,500 turbidity reducing units, repeatedly injected, did not reduce edema further. Long, nonabsorbable sutures buried in subcutaneous tissue and extending from the edematous region to normal areas, also had no effect. Gravity, compression, massage and dehydration (low salt diet and daily injection of 1-2 cc thiomerin<sup>\*</sup> during the first

(1) Surg. Gynec. & Obst. 101:25-34, July 1955

week of hospitalization) are of great value in reducing post-mastectomy edema of the arms and lymphedema praecox of the legs, and in maintaining improvement during years of supervision. Patients are encouraged to resume full activity and sports, wearing an elastic stocking or sleeve, to promote the pumping action of muscular movement on venous return and lymph flow.

► (It is curious that no operative procedure is mentioned, especially for treatment of lymphedema of the legs. A modified Kondoleon operation or the procedure described by Aird in the preceding abstract will sometimes be rewarding.—Ed.)

**Abnormalities of Human Superficial Cutaneous Lymphatics Associated with Stasis Ulcers, Lymphedema, Scars and Cutaneous Autografts** were studied by Harvey R. Butcher, Jr., and Alice L. Hoover<sup>1</sup> (Washington Univ.).

**METHOD**—The method of Hudack and McMasters, slightly modified was used for studying the pattern of the superficial cutaneous lymphatics. A tunnel was made into the upper layer of dermis with a 30 gauge hypodermic needle. Into this tunnel 0.02 ml. of 4% sky blue dye was injected through another 30 gauge needle attached to a tuberculin syringe. Slight pressure on the plunger and lateral motion of the needle facilitated the entrance of dye into the dermal lymphatics. Photographs were taken 30, 60 seconds after injection, using a Wratten A filter, an aperture of f32, an exposure of 1/1,000 second and speed flash illumination.

The patterns of the superficial dermal lymphatics outlined in the skin of the extremities of normal persons showed little variation in length, diameter and number of lymphatics in the dermal reticular network. The appearance of the reticular pattern was consistent and reproducible.

Superficial cutaneous lymphatics were usually absent in the skin about stasis ulcers, and over "hard" lymphedema (Fig 74). They were dilated overlying "soft" lymphedema and were normal over simple varicosities and with cardiac and nutritional edemas. They were initially dilated in split thickness autografts and soon established communications with lymphatics in contiguous skin. Endurance of lymphatics in a graft appears requisite for its continued survival.

Dermal lymphatics establish connections across incisions by the 12th to 14th postoperative day, with healing per primam. They were found to be few in number, and of small caliber in old dense scars of the skin after healing per secundum. The superficial lymphatics can be obliterated by sterile

(4) Ann Surg 142 633 653, October 1955

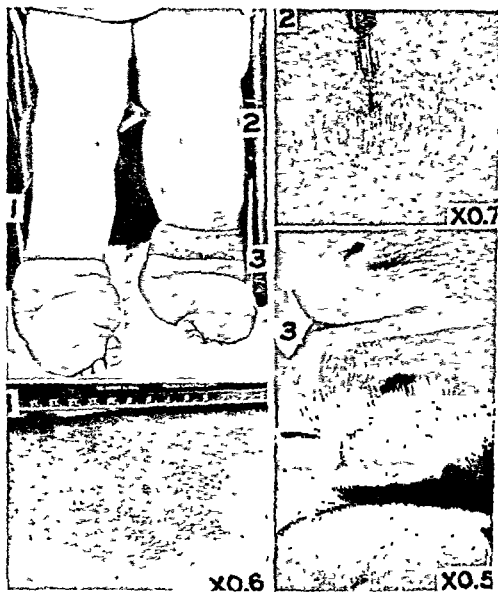


Fig 74—In chronically swollen legs superficial cutaneous lymphatics were dilated and possessed of expanded flow patterns in areas of soft lymphedema (1 and 2) No cutaneous lymphatics were injectable in the cutis subject to repeated superficial infections—area of hard lymphedema (3) (Courtesy of Butcher H R Jr and Hoover, A L. *Ann Surg* 142 633 653 October 1955)

inflammation. Absence of superficial cutaneous lymphatics is associated with hyperkeratosis, collagenous and fibrous hyperplasia of the dermis, fibrous dysplasia of the subcutaneous fat and collagenous hyperplasia of the enveloping muscular fascia.

**Surgical Management of Lesions of the Thoracic Duct: Technic and Indications for Retroperitoneal Anastomosis of Thoracic Duct to Hemiazygos Vein.** Lyman A Brewer, III<sup>5</sup>

(5) *Am J Surg* 90 210 227 August 1955

(College of Med Evangelists) states that the true incidence of all types of chylous fistulas is not known. The thoracic duct is a thin vessel, varying in diameter from 2 to 6 mm, which extends from the cisterna chyli upward along the anterior surface of the bodies of the vertebrae to empty into the venous system at the angle of junction between the left subclavian and internal jugular veins. The chyle travels from the lacteals into tiny lymphatic channels to the mesenteric lymph nodes, then through one or more intestinal trunks or afferent ducts. There is considerable variation in the number and courses of the afferent branches to the cisterna chyli. Emerging from the cisterna chyli are one and sometimes two branches of the thoracic duct. There is tremendous variation in the formation and distribution of the thoracic duct system. The thoracic duct system has the important function of carrying the chyle to the venous system. Chyle has a specific gravity of over 1.012. Its fat content is 1-3% or more and many microscopic fat globules are present. The fat is either soluble and can be stained with the usual fat dyes. Up to 4,000 cc of chyle can accumulate in one day.

Brewer reviewed 8 cases of his own and hospital records of 16 thoracic duct fistulas. The fistulas were cervical in two, thoracic in eight, thoracic and abdominal in five, thoracic, abdominal and femoral in one and abdominal in eight. Causes were surgical injury in five, external trauma in two, benign tumor in one, malignant tumor in seven, infection in one and unknown in eight.

The fundamental point in diagnosis is to make certain that the extravasated fluid is chyle. Entrance of chyle in the cervical region results in a fluctuant and painless swelling above the clavicle and absence of signs of abscess or systemic symptoms. Aspiration yields a milky fluid, and results in rapid reaccumulation of the chyle. The skin finally breaks down, forming a fistula. Lesions of the thoracic duct in the thorax lead to rapid accumulation of chyle in the pleural cavity. Extravasation of chyle occurs after aspiration, and progressive dehydration and emaciation may be fatal. Symptoms do not develop until a large amount of fluid accumulates in the pleural cavity. The lung may be collapsed and the mediastinum displaced. In the abdomen, the chyle collects first in the retroperitoneal tissues adjacent to the

sion, in either the efferent or afferent branches of the thoracic duct. Fistulas develop in the peritoneum, with pouring of fluid into the peritoneal cavity. Chylous ascites develop which must be differentiated from cirrhosis of the liver, peritonitis and cardiac failure. The chyle may escape from the abdomen along the femoral vessels and through the fossa ovalis, appear in the area of the thigh around the saphenous opening and form fistulas to the skin.

Ligation of the thoracic duct is the treatment of choice for injuries in the cervical region when simple repair is not possible. Ligation of the thoracic duct is the best treatment for injuries in the thoracic portion of the duct. Ligation is successful because the collateral channels of the duct are adequate. In the abdominal extravasations of chyle the fistula may be in the afferent ducts, the cisterna chyli or the efferent ducts. If the afferent ducts or cisterna chyli are involved the operation of choice is anastomosis of the thoracic duct to the hemiazygos vein or the azygos vein. If the abdominal thoracic duct or efferent ducts are involved, the abdominal thoracic duct should be ligated. Treatment of the fistulas in the thigh depends on the location of the chylous extravasation in the abdomen.

Of 16 patients treated by repeated aspiration, in only 1 was leakage successfully controlled. Drainage of chyle from the abdomen into subcutaneous tissue was unsuccessful in three patients and x ray therapy failed to decrease the extravasation in five of six. Ligation cured three and improved one. Anastomosis of the duct to a vein cured one patient. Spontaneous recovery occurred in two, and two were cured by miscellaneous methods.

Of 24 patients 9 were cured, the mortality was probably 11 (46%). Malignant disease was present in seven patients and no hope of permanent cure was expected. Mortality can be lowered and rate of permanent cure can be improved by careful ligation of lesions above the diaphragm and anastomosis for lesions below the diaphragm, if feasible.

## ABDOMEN—GENERAL

**Hydrocortisone Acetate Applied Intraperitoneally** in rabbits was used by Lis Zachariae<sup>6</sup> (Copenhagen) to test its inhibitory effect on adhesions produced by serosal injury and on re-formation of surgically separated adhesions and its effect in the presence of infection and after intestinal anastomoses.

The inhibitory effect on adhesions produced in 10 rabbits by serosal injury was similar to that obtained in earlier experiments in which adhesions were produced with talc. In six rabbits, inhibitory effect of hydrocortisone on re-formation of surgically separated adhesions was not so pronounced but was definite, since extensive adhesions did not reappear. Injury in these cases was more severe than in the previous group, often entailing severe serosal injury and hemorrhage.

Mild infection, produced by perforating the appendix, was treated with hydrocortisone in five rabbits. Three died within the first week of diffuse peritonitis, one showed clinical signs of peritonitis but recovered and one was entirely unaffected. None of five controls showed peritonitis, though four had periappendicular abscesses, two of which perforated to the abdominal surface. Of five rabbits with massive infection (caused by cutting off the tip of the appendix) treated with hydrocortisone, four died the first week of diffuse peritonitis and one remained unaffected. Two of five controls died the first week of peritonitis and the others had large periappendicular abscesses, two of which perforated to the abdominal surface.

Intestinal anastomosis was performed in 10 rabbits. Of the five treated with hydrocortisone, three died of diffuse peritonitis the first week; autopsy showed insufficient suture. After six weeks, both survivors had a sufficient anastomosis, in one it was surrounded by a few adhesions and in the other, large portions of intestinal wall on both sides showed severe phlegmonous inflammation. Three control animals had sufficient anastomoses surrounded by ample ad-

(6) *Acta endocrinol.* 19:269-278, July, 1955.



hesions, whereas two exhibited small, encapsulated abscesses at the sites of sutures

These experiments demonstrate that, by inhibiting development of adhesions, hydrocortisone acetate, like other substances of the cortisone group, prevents encapsulation of inflammation and increases the spread of infection

► [Obviously, therefore, hydrocortisone should not be used to prevent abdominal adhesions—Ed]

**Plasmin in Prevention of Adhesions: Preliminary Report**  
Evert Gustavsson, Birger Blomback, Margareta Blomback and Per Wallen<sup>7</sup> (Karolinska Inst, Stockholm) studied the use of the fibrinolytic principle of the blood, plasmin, in prevention of adhesions in rabbits. Plasmin is present in the blood as a pre-enzyme, plasminogen, which can be slowly activated as a kinase in the tissue detritus. More rapid activation is produced by many other kinases, particularly those from certain micro organisms. The kinase from some hemolytic streptococci (streptokinase) activates human plasminogen almost exclusively, while kinase from staphylococci activates the plasminogen of the monkey, dog and rabbit.

A segment of the cecum and the abdominal wall of rabbits were deperitonealized, lacerated and placed in direct contact with each other. In 26 animals, 400 mg of fraction II and III from human plasma (plasminogen) and 65,000 units of streptokinase were placed in the intraperitoneal cavity. The animals were killed after 7-24 days. Of the 26, 16 had no adhesions, 6 had one to two thin strandlike adhesions and 4 had extensive adhesions. All of 3 animals given 65,000 units of streptokinase alone and 20 control animals similarly treated had extensive adhesions.

Uterotomy was performed in 15 animals (5 controls) and 7 were given plasmin intraperitoneally by abdominal puncture or through a catheter inserted in the abdominal wall. When the abdomen was reopened 14-25 days later, the uterotomy was open in three and closed in four. In three in which the plasmin was inserted through a uterine catheter, the uterotomy was open in two and closed in one. The five controls had closed uterotomy incisions.

The study demonstrates that plasmin can prevent formation of peritoneal adhesions in the rabbit. Streptokinase

alone is not effective, since it does not activate the plasminogen of the rabbit to any great extent. Better results may be anticipated with streptokinase alone in man. Preliminary results in the cat, in which plasminogen is also easily activated by streptokinase, showed that streptokinase did not prevent adhesions, probably because the plasminogen content of the abdomen is too low or the inhibitor activity is too high. Plasmin may be used in plastic operations on the fallopian tubes for treatment of sterility.

**Isolated Lipodystrophy, Form of Mesenteric Tumor** appears to be a unique entity, although it resembles Whipple's disease, Weber-Christian disease with systemic involvement, sclerosing lipogranuloma and traumatic or pancreatic fat necrosis. These masses must also be differentiated from true fat tumors, lymphosarcoma, tuberculosis and other less common conditions. Biopsies should be taken of mesentery, bowel and mesenteric lymph nodes. Surgical resection usually is not feasible, as the process tends to surround major mesenteric vessels. The lesion is slowly progressive and probably self-limited, there is no evidence that the process later involves other tissues.

In five cases observed by Jackson T. Crane, Mary Jane Aguilar and Orville F. Grimes<sup>8</sup> (Univ. of California), a massive tumor extended from the root of the mesentery to within a few centimeters of the intestine proper, with thickness to 9 cm. The zone immediately adjacent to the intestine was unaltered. The remaining diffusely involved mesentery was rubbery firm, mottled, opaque and nongreasy, mottled gray to yellowish orange. The cut surface showed multiple yellowish orange nodules, 1 cm. to several centimeters in diameter. Microscopically, fat cells were most prominently involved about the periphery of fat lobules. In early stages, individual fat cells were small, with opaque, granular and faintly basophilic cytoplasm and a central nucleus. Later, a mild focal lymphocytic infiltration (Fig. 75), probably indicating inflammatory reaction to degenerating fat, and perilobular condensation of fibrous tissue appear. Only rarely and in small foci was lipogranulomatous change evident (Fig. 76).

Pathologic findings suggest that initial proliferation of mesenteric fat induces a change in fat cell metabolism. Fat

(<sup>8</sup>) *Am J Surg* 90:169-179, August 1955.

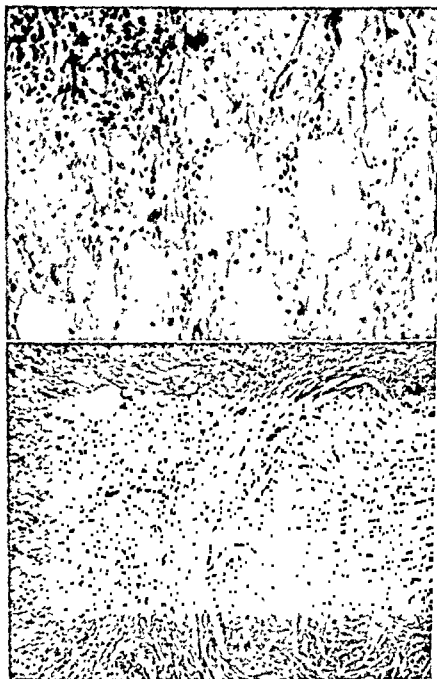


Fig 75 (top) —Small infiltrate of mononuclear cells (upper left) in broad field of abnormal fat cells

Fig 76 (bottom) —Focus of "lipogranulomatous inflammation" (right) is present as discrete nodule in large field of abnormal fat cells. Centrally, nodule is comprised of cellular debris and acicular clefts (crystalline material) about which is a collar of phagocytes, giant cells and lymphocytes

(Courtesy of Crane, Jackson T., *et al*. *Am J Surg* 90:169-179, August, 1955)

cells, particularly those of the more ischemic peripheral lobules, lose their ability to absorb fat and their lipolytic activity is compromised. These altered cells undergo structural changes, and may progress to breakdown, liberating

fatty acids and exciting focal inflammation and fibrosis

Patients exhibited no symptoms directly attributable to the palpable abdominal masses. The diagnosis was established at exploratory laparotomy in three and post mortem in the other two. One died of cardiovascular disease before operation could be performed, and in a case of systemic amyloidosis, the mesenteric mass was an incidental autopsy finding.

**Serum Amylase and Acute Abdominal Disease.** W. Burnett and J. D. Ness<sup>9</sup> (Univ. of Aberdeen) determined the serum amylase, using the Somogyi method, in 350 consecutive patients with acute abdominal pain. This method measures the rate of destruction of a standard solution of starch by serum amylase, being recorded by the disappearance of the starch-iodine blue color as hydrolysis progresses. A control series of 50 estimations in normals gave a range of 62-177 Somogyi units, with an arithmetic mean of 115 and a standard deviation of  $\pm 33$ . The serum amylase value was over 400 units in all of 14 patients with acute pancreatic disease (over 1,000 units in 13), in 2 of 23 patients with acute cholecystitis, in 8 of 31 with perforated peptic ulcer (over 1,000 units in 2), in 3 of 35 with intestinal obstruction (over 1,000 units in 2), in 2 of 149 with acute appendicitis, and in 3 of 98 with miscellaneous diseases, mostly genitourinary and gynecologic patients.

Among the 14 patients with pancreatic disease, the initial serum amylase values ranged from 1,200 to 6,000 units in 12 with acute pancreatitis. Very high values are usually found in the first 24 hours of the disease. The level tends to fall abruptly after 24-36 hours and then more gradually until normal levels are reached in 4-5 days. High serum amylase values are not pathognomonic of pancreatitis, since they were also found in perforated peptic ulcer and intestinal obstruction in four patients. The test, however, is valuable in differential diagnosis of acute pancreatitis and acute cholecystitis and should be done in every case of acute abdominal pain.

It is postulated that peritoneal absorption is the cause of increased serum amylase in perforated ulcer and that absorption of pancreatic amylase in the intestine may occur through the damaged bowel wall or the peritoneum in intes-

(9) Brit. M. J. 2 770 772 Sept. 24 1955

tinal obstruction With the altered bacterial flora occurring in appendicitis and other abdominal infections, enough bacterial amylase may be absorbed through areas of increased vascularity in the affected region to produce a small increase in serum amylase

---

## THE LIVER AND SPLEEN

**Total Right Hepatic Lobectomy for Cancer of Gallbladder Report of Three Cases** If unsuspected cancer is found at operation for simple cholecystectomy, George T Pack, Theodore R Miller and Richard D Brasfield<sup>1</sup> (Memorial Center for Cancer, New York) believe that it is better to do a total right hepatic lobectomy at that time Any operation short of this, such as palliative cholecystectomy by enucleating the gallbladder from its bed, greatly complicates performance of total lobectomy later Advanced cancers usually are inoperable by general standards though possibly not through the medium of total right hepatic lobectomy

Fears and hazards of hemorrhage in this procedure have been dispelled by preliminary ligation of the right branches of the hepatic bile duct, hepatic artery and portal vein within the porta hepatis The more adequate exposure afforded by a right thoracoabdominal incision has made the operation safer and easier In man the left lobe comprises only 20-22% of the total liver substance yet it is sufficient to assume all the functions of the liver, once the entire portal venous circulation is shunted into it

Two of the three patients had had previous surgery for gallbladder cancer (one of these had had simple cholecystectomy and intensive postoperative irradiation), which made the operations difficult The present postoperative course was unremarkable Serum albumin 50 Gm daily was given for 10 days and 100 mg cortisone daily stimulated the appetite and rapid convalescence Hepatic function has been within normal limits postoperatively The other patient had intermittent digestive complaints after the present operation (total right hepatic lobectomy), and evidence of intra-thoracic metastases appeared Limited autopsy 5½ months

(1) *Ann Surg* 142 6-16 July 1955

later showed no metastases in the left lobe which had undergone regenerative hyperplasia and weighed almost 500 Gm. The third patient had had no previous operation, but extensive metastases to periportal, hepatoduodenal and retroduodenal lymph nodes made the dissections arduous and the prognosis ominous. Due to ileus, he did not receive immediate postoperative high caloric and high protein feedings and died on the seventh postoperative day. At autopsy, the left hepatic duct was intact, and the left lobe of the liver (weighing 400 Gm) was an estimated 50% larger than at the end of the operation.

Among the authors' patients, the one who has lived longest (two years) is a man, weighing 200 lb and working, who had had a huge granuloma involving the entire left lobe.

► [At present one can only withhold judgment on the feasibility of this operation until after more time has elapsed and more patients have been operated on.—Ed.]

**Postoperative Course Following Total Right Hepatic Lobectomy** Abdol H. Islami, George T. Pack, Theodore R. Miller, Parker Vanamee, Henry T. Randall and Kathleen E. Roberts<sup>2</sup> (Memorial Center for Cancer and Sloan-Kettering Inst., New York) report on four patients in whom the operation was performed for malignant tumors. The amount of liver removed was estimated at 70-80%. There were alterations immediately after surgery in all liver functions, indicative of parenchymatous as well as obstructive changes. Serum bilirubin increased during the postoperative interval and returned to normal within three weeks. The increased portal congestion of the remaining left lobe immediately following removal of the right lobe is sufficient to occlude the intrahepatic ducts temporarily by extrinsic pressure. Transient jaundice is therefore the rule. Cephalin flocculation and thymol turbidity increased in two patients, in the remaining two these values were abnormal before surgery. One patient had an immediate decrease in alkaline phosphates, cephalin flocculation and thymol turbidity. Two had slightly elevated but normal prothrombin times, and none had any clinical evidence of abnormal bleeding during the recuperative interval.

All patients had a profound decrease in both the albumin and globulin fraction of the total protein levels. Three had

a slight decrease in plasma sodium and phosphate levels. Blood ammonia levels were not significantly elevated (Tests in dogs following removal of 70% of the liver showed similar ammonia tolerance.)

Vitamin A levels, measured in two patients, were found to be normal after surgery. The serum transaminase level was slightly elevated in all patients, but this increase is observed after surgery in all patients.

► [These comparatively slight changes following the removal of approximately 70 to 80% of the liver are not surprising in view of the findings of Mann many years ago in his classic work of removing large portions of liver and even the whole organ in dogs.—Ed.]

**Right Lobectomy of Liver in Children** is feasible, as demonstrated by H. William Clatworthy, Jr., and E. Thomas

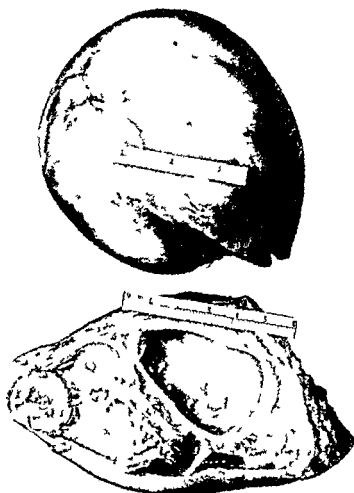


Fig. 77 (top) —Resected right hepatic lobe.  
 Fig. 78 (bottom) Section of specimen shows multilocular cystic structure of lymphangoma.  
 (Courtesy of Clatworthy, H. W. and Stiles, F. T. Surgery 39:850-859 May 1956.)

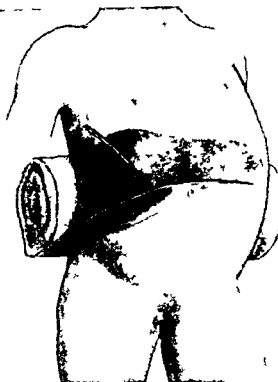
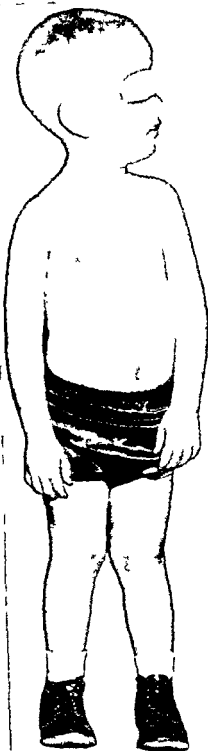


Fig 79 (left) —Patient two years after total right hepatectomy for lymphangioma of liver. Note well healed scar.

Fig 80 (above) —Supraumbilical transverse incision is joined later by incision through 8th right intercostal space.

(Courtesy of Clatworthy, H. W., and Boles, E. T. *Surgery* 39:850-859, May, 1956.)

Boles, Jr.<sup>3</sup> (Ohio State Univ.) in two instances. In a boy, 17 months, with the right lobe largely replaced by a hepatoma, the postoperative course was complicated by bile



peritonitis and jaundice After recovery of good health and vigor, the child died after a brief illness 2½ months post operatively The second child had an uneventful recovery after resection for a massive lymphangioma (Figs 77 and 78) at age 5 months and has developed normally (Fig 79)

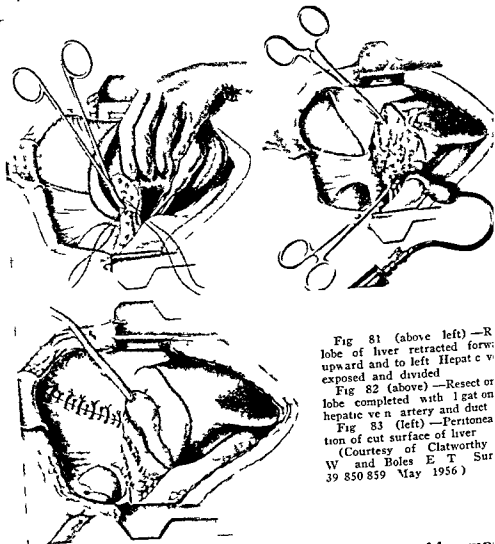


Fig 81 (above left) —R lobe of liver retracted forward and to left Hepatic v exposed and divided

Fig 82 (above) —Resect or lobe completed with ligat on hepatic ven artery and duct

Fig 83 (left) —Peritonea tion of cut surface of liver (Courtesy of Clatworthy W and Boles E T Sur 39 850 859 May 1956)

Adequate hepatic function without demonstrable impairment may be expected to follow right lobectomy

**TECHNIC**—Satisfactory exposure for resection of the right requires a combined thoracoabdominal approach Complete abdominal exploration is performed through a transverse supraumbilical or costal incision This is then joined by a thoracic incision in the eighth intercostal space incising the diaphragm down to the cava thus widely opening the right thoracoabdominal area (Fig Hemostasis is achieved by dissection of the hilus of the liver ligation and division of right hepatic duct right hepatic artery right portal vein The gallbladder is enucleated from its liver

but purposely not removed since it is used later in retrograde injection of the biliary tree. The right lobe can then be rotated upward and to the left, resting partially in the right chest. Access is thus obtained to the 6-10 short hepatic veins running from the right lobe into the vena cava, which are individually exposed, ligated and divided to avoid serious hemorrhage or air embolism later (Fig. 81). Additional hemostasis from free edge of left lobe is obtained by cross-clamping the remaining hepatoduodenal ligament for a few moments with a Potts clamp. Visible blood vessels and bile ducts are individually clamped and ligated as the liver is transected with a scalpel. Placement of a row of mattress sutures to left of plane of division before resection may be advantageous.

Bile leakage is further minimized by placing a small catheter into the gallbladder, and, with the common bile duct temporarily occluded below the cystic duct, performing a retrograde injection of the intrahepatic biliary tree via the cholecystotomy with saline solution colored with methylene blue (Fig. 82). Additional open biliary radicles on the raw liver surface are thus detected and ligated. Repertonealization of the raw surface is accomplished in so far as possible with the falciform ligament, stretched-out gallbladder and mobilized peritoneum overlying the kidney. Penrose drains are left adjacent to the divided liver surface (Fig. 83).

**Surgical Experiences in Portal Hypertension: Review of 19 Cases from Brooke Army Hospital.** Donald G. Fahy, Jacob F. Schirmer and Warner F. Bowers<sup>4</sup> (Fort Sam Houston, Tex.) believe that the only beneficial effect of portacaval shunting operations is reduction of portal venous pressure, and this therapy for esophageal hemorrhage, even from esophageal varices, cannot be expected to be efficacious if the hemorrhage is due to causes other than portal hypertension. An esophageal varix pressure of more than 250 mm. water, on the other hand, is a definite indication of portal hypertension, and a patient with this finding should be aided by a shunting procedure. Treatment of esophageal hemorrhage by esophageal vein ligation, esophagogastratomy or other operations aimed directly at obliteration of the offending varix should be reserved for cases in which portal hypertension does not play a part, has been controlled or is not amenable to correction by portacaval shunting operations, or in the occasional case in which hemorrhage cannot be controlled by conservative measures.

Surgery for portal hypertension was done in 16 males and 3 females, average age 42, from August 1952 through July 1954. In three portal hypertension was caused by extrahepatic block; one of these also had biliary cirrhosis. Of the

(4) A M.A. Arch Surg. 72:583-594, April, 1956.

16 patients with portal hypertension on the basis of intrahepatic portal block, 15 had Laennec's cirrhosis, of whom 8 were alcoholics, and 1 had schistosomiasis. In only two was the preoperative esophageal varix pressure less than 250 mm water. Ascites was present in 3 patients in the intrahepatic group, and in 15, hemorrhage had occurred. In the extrahepatic group, two had bled and in none was ascites a factor. A portacaval shunting procedure was planned for 18 patients, but technical difficulties led to abandonment of the procedure in 1 and only exploration was performed in 1 because the portal pressure was only 194 mm water, despite preoperative esophageal varix pressure of 305 mm water. Both patients died in liver coma, without hemorrhage. In two only splenectomy was done.

Shunting procedures were done in 14 instances, spleno-renal and side-to-side portacaval anastomoses were performed once each and 12 patients had end-to-side portacaval anastomoses. Preoperative pressures from the esophageal varices ranged from 210 to 425 mm water and after the shunting procedure, from 120 to 185 mm. In five no varices could be visualized at postoperative esophagoscopy. Varix pressures measured preoperatively averaged 320 mm water. The postoperative mean varix pressure was 127 mm water. The mean preshunt pressure in the portal vein in 10 patients was 396 mm and the mean postshunt pressure was 283 mm water. In general the postshunt decrease in pressure was more marked in the varix than in the portal vein, immediately after the operation, but it is thought that the portal pressure decreases further later.

Four of the patients who had the shunt operation died. In one the shunt was closed at autopsy three months postoperatively, although the portal pressure had dropped from 418 to 280 mm water. One patient died of recurrent hemorrhage from esophageal varices. Both deaths were hastened by the operation. Two patients died 14 months postoperatively; neither had bled from varices postoperatively.

Effective portal pressure reduction was produced in all but one in whom thrombosis of the major veins of the portal system precluded establishment of an adequate shunt. This patient subsequently had partial esophagogastrectomy and had no recurrence of hemorrhage. In the 19 patients, counting early and late deaths from all causes and including

those in whom exploration only was done, the total fatality rate was 37%, with an 18 36 month follow up

Ligation of Portal Vein was performed by Franz F. Niedner and Wolfgang Mattes<sup>5</sup> on a patient having surgery for biliary tract obstruction and infection, six weeks after cholecystectomy had been done elsewhere. This is the fifth portal ligation reported, with survival of the patient. In earlier instances, compression of the portal vein by scar tissue or tumors had led to formation of collateral vessels, hence circumstances were more favorable for ligation of the portal vein. However, Child concluded from experiments on monkeys that a previously uninjured and intact portal vein could be ligated without risk to life in man also.

Man during portal vein ligation in October 1950 received 4 L blood and afterward 1 000 cc fluid intravenously and two additional transfusions of 500 cc. He was pulseless for some time, blood pressure was 70/55, breathing was superficial and there was slight cyanosis. By evening blood pressure had increased slowly to 100/75, and pulse was palpable but still weak and rapid. The next day, the circulation was fully stabilized. There was little disturbance postoperatively that could be attributed to portal ligation, but serious complications resulted from biliary infection and spilling of bile into the intestines. After a stormy course signs of portal hypertension began to appear, and the spleen became enlarged and painful in ensuing months. Portal caval anastomosis was performed in October 1951. Postoperative course was smooth and uneventful with prompt recovery.

Afterward the icteric tinge decreased and finally disappeared. The general condition improved so much within a year that he was able to return to work full time. Symptoms resulting from biliary tract infection eventually disappeared completely. Five years after portal ligation he was well and energetic with no hypoglycemia and no disturbance of sugar metabolism. There was no evidence of portal hypertension or cirrhosis. The bromsulphalein<sup>®</sup> test showed only slight liver damage which could not definitely be attributed to portal ligation as some liver insufficiency was evident before the first operation.

This case demonstrates that ligation of the portal vein is possible in man if sufficient protection is provided by transfusions and intravenous infusions so that the right heart retains a normal volume of circulating blood. Within a short time circulation is re-established as after ligation of the vena cava. The case confirms experimental work showing that ligation of the portal vein does not lead to ascites, which is believed to result rather from obstruction of blood flow between the heart and central hepatic veins. Congestion

(5) Deutsche med. Wchnschr. 81:438-462, Mar. 30, 1956.

of the liver, not of the portal venous system, is the decisive factor in the pathogenesis of ascites

**Diagnosis of Portal Hypertension · With Notes on Treatment.** J. Garrott Allen and Louis R. Head<sup>6</sup> (Univ of Chicago) point out that in patients over 30, massive bleeding into the upper gastrointestinal tract arises from portal hypertension in only 10-15% of cases. In children and young adults, however, massive hematemesis comes much more often from the bleeding varices of portal hypertension than from peptic ulcer.

The outstanding feature in history of portal hypertension is hematemesis. The varix which bleeds for the first time bleeds massively more often than does peptic ulcer. The bleeding varix in the adult with cirrhosis is more likely to be fatal for any given episode than is a single episode of bleeding in a child. Viral hepatitis, whether infectious or serum hepatitis, is often the only preceding fact to explain cirrhosis and its consequences, i.e., portal hypertension, bleeding and ascites.

Important physical findings in portal hypertension are hepatomegaly, splenomegaly and ascites; these suggest that bleeding is from varices rather than from ulcer. Portal hypertension can be strongly suspected on the basis of secondary manifestations. The caput medusae is good evidence of extensive collateral circulation and is more common than spider nevi. Cutaneous collaterals on the anterior surface of the abdomen can occasionally be demonstrated better by infra red photography than by direct view, since edema tends to obscure them. These are diagnostic of portal obstruction but not necessarily of portal hypertension. Ascites is often present in adults with cirrhosis but is seldom seen in children and young adults with portal hypertension. Loss of muscular tone and substance is characteristic, due to dehydration and also to impairment of protein metabolism. If the liver is palpable and tender the possibility of recent right heart failure or of recurrent hepatitis should be considered. A nodular liver favors diagnosis of latent cirrhosis or tumor. Splenomegaly is nearly always present in portal hypertension, with or without liver enlargement.

Presence of portal hypertension is inferred by fluoroscopic demonstration of esophageal or gastric varices, although

negative findings do not exclude it. A series of films over several years often shows clearly an increase in size and number of varices. After shunting procedures, varices remain but become less conspicuous when intraluminal pressure is relieved. At fluoroscopy, search for gastric varices is important, because these are often the source of severe bleeding that cannot be controlled by tamponade. Splenography has proved a valuable diagnostic aid when shunting procedures are to be performed. Esophagoscopy is useful diagnostically for detecting varices at a time of acute upper gastrointestinal hemorrhage. It is often the only procedure that can be used successfully. If varices are not found, gastroscopy may be useful in some patients.

No specific laboratory test will demonstrate presence or absence of portal hypertension, but several are useful as indexes of severe liver disease and of secondary hypersplenism. These include the bromsulphalein\* test for measurement of excretion, serum albumin determination as an index of protein metabolism, tests for prothrombin activity, esterification of cholesterol (impaired only in advanced liver disease) and cephalin flocculation, and needle biopsy of the liver. The last should be used whenever possible if the diagnostic nature of liver disease is important to selection of treatment. Manometric measurement of portal pressure, the only means of definitive diagnosis of portal hypertension, should be performed as soon as the abdomen is opened. A value of 230 mm. in excess of water pressure is diagnostic of portal hypertension; readings of 500-600 mm. water are occasionally found.

Occasionally the enlarged spleen in portal hypertension may cause anemia, leukopenia and thrombocytopenia, alone or in combination, which require splenectomy. This should not be undertaken, however, unless the surgeon is prepared to perform a splenorenal shunt at the same time.

Surgical treatment of a bleeding varix becomes necessary if tamponade is ineffective, but every reasonable effort should be made to avoid intervention during acute hemorrhage. Absorption of blood proteins from extensive and continuing hemorrhage into the upper intestinal tract may cause ammonia intoxication; this argues strongly for early control of bleeding and for a partial diversion of portal blood, by splenorenal shunt rather than total diversion of

portal blood, as occurs in end-to-side portacaval anastomosis. Suturing esophageal varices and partial esophagogastrectomy have been used to achieve surgical hemostasis when bleeding cannot be arrested.

The authors have also used gastric bisection and devascularization of upper gastric segment, including the vasa brevia of the spleen, with or without splenectomy. Phrenic veins as well as the coronary vein and left gastric artery are ligated and divided. Line of bisection must be high enough to prevent necrosis of the upper segment. The lower segment receives blood supply from the right gastroepiploic artery and vein. Pyloroplasty or gastroenterostomy should also be performed. Of four patients so treated, none bled again, although two died during the immediate postoperative period of pneumonia. One lived 10 months and died in hepatic failure without bleeding and the fourth was alive and well without hemorrhage after 3 years.

**Bacteriologic Study of Portal Vein Blood in Man** is reported by William E. Schatten, John D. Desprez and William D. Holden<sup>7</sup> (Cleveland). Organisms were cultured from portal vein blood of 8 of 25 patients from whom blood was taken at laparotomy. Six of the positive cultures showed gram-positive cocci. Though most patients from whom blood was taken had biliary tract disease, it is believed that no relation exists between the disease process and presence of organisms in portal vein blood because samples were obtained for culture before the biliary tract was opened. Two of four patients given antibiotics 5-10 days preoperatively had positive portal vein cultures. Cultures of peripheral vein blood were not positive in any instance.

The study demonstrates that bacteria pass from the gastrointestinal tract to the liver via the portal vein. Why gram-positive cocci pass the gastrointestinal barrier in greater numbers than other bacilli is not known. Discovery of continual passage of intestinal bacteria to the liver explains why antibiotics are valuable after hepatic artery ligation and in treatment of acute and chronic diseases in which severe hepatic insufficiency occurs. That changes of acute hepatic necrosis are usually more severe in the left lobe is interesting because this lobe receives blood from the colon, the site of greatest bacterial growth. There is rationale

for sterilizing the gastrointestinal tract in all patients with hepatic function significantly impaired

**Portacaval Anastomosis: Rationale, Indications and Technique** are discussed by George A. Hallenbeck<sup>8</sup> (Mayo Clinic). The purpose of shunts between portal and caval venous systems is to provide sufficient direct outlet for portal blood to prevent serious bleeding from natural collateral channels, including esophageal varices. Two types of shunts best meet these requirements: in one, the spleen is removed and the end of the splenic vein is anastomosed to the side of left renal vein, the left kidney being preserved; in the other, the portal vein is anastomosed directly to the vena cava, either end to side, or, less often, side to side.

When a venous anastomosis is contemplated, the first task is to determine whether portal obstruction is intrahepatic or extrahepatic. If liver disease is absent, portal obstruction is usually extrahepatic, and the portal vein is unsuitable for shunting. The final decision is confirmed by portal venography, performed just before operation.

Splenectomy with splenorenal anastomosis is the treatment of choice for patients with extrahepatic portal obstruction who have bled from esophageal varices, provided there is no other contraindication, or the patient is not a small child. Patients with cirrhosis should have good enough hepatic function so that the risk of operation is less than that of conservative treatment. The ideal cirrhotic patient for shunting is one with adequate liver function who has bled from varices but has never had ascites. One who has bled and later has transient ascites that responds to medical treatment is usually suitable. A serum albumin level less than 3 Gm/100 cc, chronic ascites, failure of prothrombin time to return to within four seconds of normal after vitamin K, jaundice, a cephalin cholesterol flocculation of 3+ and 4+ and pronounced sulfobromophthalein retention are unfavorable signs. Elimination of patients who cannot withstand operation and proper preparation of those in which liver function can be improved are extremely important in obtaining an acceptable postoperative mortality.

Either splenectomy with splenorenal anastomosis or direct portacaval shunt is technically possible in most patients with intrahepatic portal obstruction. Side to side portacaval



anastomosis, feasible in some slender patients, is often impossible without venous grafting in others, either because veins lie too far apart or a hypertrophied caudate lobe of the liver lies between them. A side-to-side shunt might also allow retrograde escape through the portal vein and shunt of blood reaching the liver via the hepatic artery. Hence for direct portacaval shunt, end-to-side anastomosis is preferred. Since caliber and disposition of splenic and renal veins are less constant than in the portal vein and vena cava, direct portacaval shunt is easier to perform and more consistently provides good decompression of the portal system. End-to-side portacaval shunts are used increasingly often, unless the large size of the spleen and significant hypersplenism make its removal obligatory.

Patients with hepatic disease receive supportive treatment postoperatively, including oxygen for 24-48 hours, transfusion of whole blood, if indicated, and continuous slow intravenous administration of glucose (10%) with vitamins, including vitamin K. Anticoagulants are not used routinely, but heparin may be given if vague abdominal symptoms indicate the presence of portal thrombosis.

The hospital mortality in 14 splenorenal and 29 portacaval shunts in patients with hepatic disease was 16.3%. No postoperative deaths occurred in 4 with intrahepatic portal obstruction without cirrhosis or impaired liver function nor in 11 with extrahepatic portal obstruction who had splenorenal or direct portacaval shunts.

**Portal Hypertension** Surgical methods aimed at providing a larger diversion of portal blood to prevent esophageal hemorrhage in cases of cirrhosis and Banti's disease with esophageal varices are described by Cornelius E. Sedgwick and Charles M. Parrish<sup>9</sup> (Lahey Clinic). Operation is not indicated in cirrhotic patients without varices, or patients with varices that have not bled. A splenorenal shunt may be indicated in a patient with secondary hypersplenism who has not bled but who requires splenectomy. Patients with esophageal bleeding without ascites constitute the most favorable group. Mortality associated with shunt procedures in chronic ascites, a sign of advanced hepatic impairment, is usually prohibitive although sometimes operation can be performed without undue risk after prolonged medical

(9) S. Clin. North America 35:667-678, June 1955.

therapy. The most reliable laboratory criteria indicating tolerable surgical risk are serum albumin over 3 Gm./100 cc.; bromsulphalein\* retention under 15%; prothrombin time 60% or greater, and cephalin flocculation 1-2+. Choice of a shunt operation depends to some extent on portal venous anatomy, which can be determined by splenoportography.

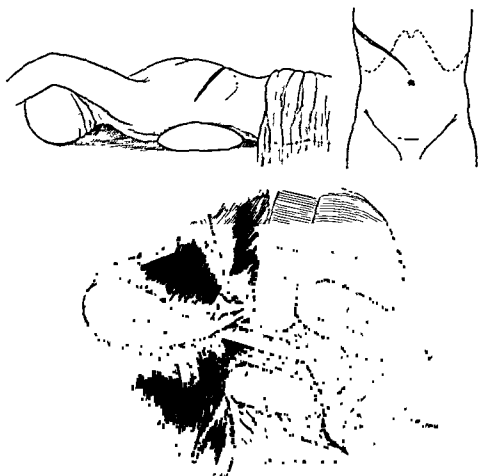


Fig 84 (top) —Long curved thoracoabdominal incision with patient in semilateral position

Fig 85 (bottom) —Postparietal peritoneum is incised, vena cava and portal vein are exposed and duodenum is mobilized

(Courtesy of Sedgwick, C. E., and Parrish, C. M.: *S Clin. North America* 35: 667-678, June, 1955.)

**TECHNIC.**—After the patient is anesthetized and intubation is done, splenoportogram is obtained by percutaneous injection of 50 cc. of 70% urokon® or diodrast® through the eighth or ninth interspace directly into the spleen. If films are unsatisfactory, diodrast® is injected directly into the portal system through the cannula used for determination of portal pressure, before continuing with one of the shunt procedures.

**Portacaval shunt.**—The best exposure is obtained, with the patient in a semilateral position, through a long oblique thoracoabdominal

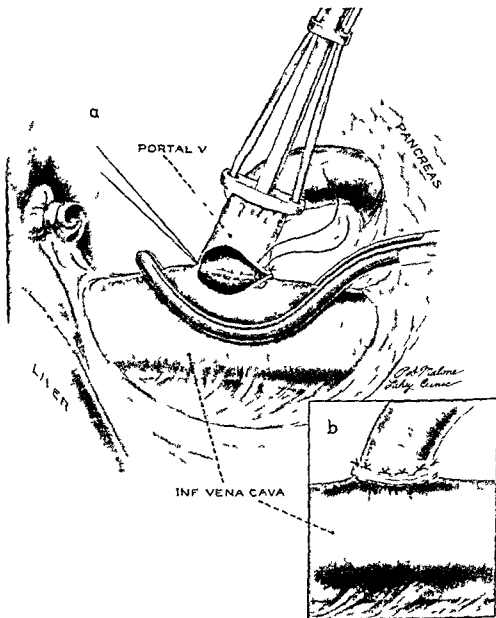


Fig 86—Portocaval anastomosis note high ligation of portal vein and Linton clamp on vein. Poster or aspect of vena cava is not completely immobilized. Clamp on vena cava produces partial occlusion. (Courtesy of Sedgwick C E and Parrish C M. S Clin North America 35 667 678 June 1955)

incision from just above the umbilicus through the eighth interspace, well posterior to the lumbar muscles (Fig 84). The diaphragm is divided, the lung packed above and the liver, which is usually large, is displaced upward and partially into the chest. Manometric portal pressure readings are obtained, portal portography performed, if necessary, and if the portal vein is visualized the stomach and small bowel are packed to right and cephalad. Hepatic flexure is freed and retracted downward. The posterior parietal peritoneum is excised laterally and dissection is continued medially, exposing the

vena cava at about the level of the renal vein (Fig. 85). About two thirds of the anterior circumference of the vena cava is mobilized. Lateral and posterior lumbar veins are not disturbed. Portal vein is exposed (after excision of lymphoid tissue overlying the porta hepatis, if necessary) and mobilized, along with the duodenal sweep and head of the pancreas; sometimes a liver lobe separates

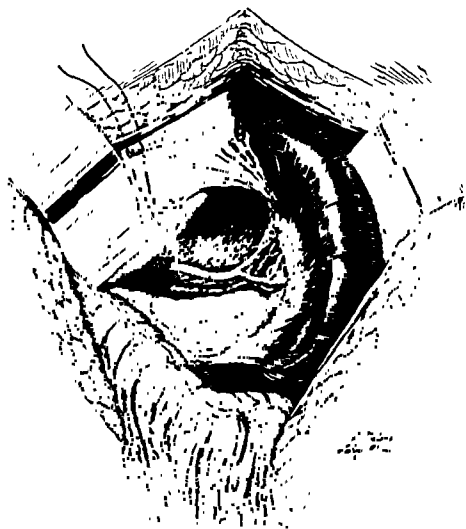


Fig. 87—Lesser sac is opened, greater curvature of stomach freed and splenic artery ligated (Courtesy of Sedgwick, C. E., and Parrish, C. M.: *S. Clin. North America* 35 667-678, June, 1955)

the portal vein and vena cava by as much as 7 or 8 cm. The portal vein is then ligated and transfixed as high in the hilus as possible, with the clamp devised by Linton (Fig. 86). Anastomosis is made with interrupted everted sutures of 5-0 Deknatel. Good pulsation is felt as portal blood rushes into the vena cava. A drain is placed in Harrison's pouch, a catheter in the chest, and abdomen and chest are closed.

*Splenorenal shunt.*—The same thoracoabdominal incision is used except that it is on the left side. After portal pressure is recorded,

the lesser sac is entered, stomach retracted upward and completely freed along the greater curvature, and all short gastric arteries are divided (Fig 87) Transverse colon and splenic flexure are separated from the splenic pedicle The splenic artery is then isolated along the superior border of the pancreas and spleen is delivered into

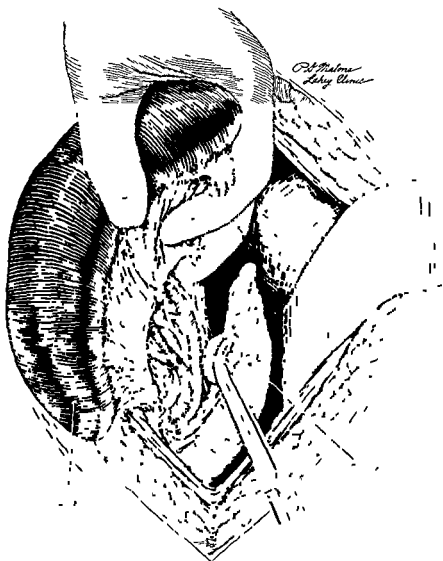


Fig 88—Spleen is completely mobilized and retracted out of wound and splenic vein is isolated from behind (Courtesy of Sedgwick C E, and Parrish, C M S Clin North America 35 667 678, June, 1955)

wound The splenic vein is approached from behind (Fig 88) and separated from pancreas The spleen is not removed until an appropriate length of splenic vein is well mobilized Bleeding from splenic vein is controlled by a bulldog vascular clamp or the Linton clamp Then posterior parietal peritoneum is divided just medial to the hilus of the kidney, which is not mobilized The renal vein is isolated for 4-5 cm with ligation of small tributaries Heavy silk ties control

renal venous flow while anastomosis is performed (Figs. 89 and 90) with simple interrupted everted sutures of 5-0 Deknatel. After posterior sutures have been tied, clamp on the splenic vein should be released momentarily to flush out clots. The anterior row of sutures

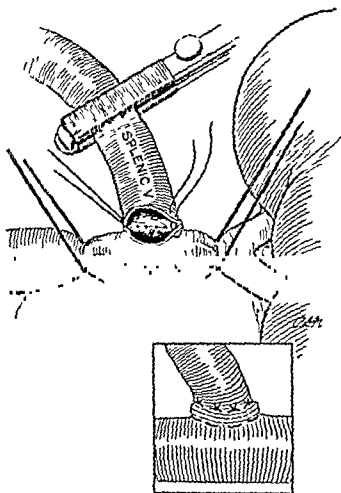


Fig 89 (top) —Renal vein is controlled with heavy silk  
 Fig 90 (bottom) —Interrupted everting sutures are utilized for the anastomosis  
 (Courtesy of Sedgwick, C E, and Parrish, C M S Clin North America 35 667  
 678, June, 1955)

is then quickly placed. A drain is placed in the region of the pancreatic tail and a catheter in the chest.

Postoperatively, care is taken to prevent distention and reaccumulation of fluid. Usual precautions following thoracotomy are used. Anticoagulants are not used. Oxytetracycline, 500 mg/day, is given for five or six days. Patients are encouraged to take food by mouth as soon as possible after operation.

**Surgical Treatment of Banti's Syndrome.** V. Paltia and M. Sulamaa<sup>1</sup> (Univ. of Helsinki) report on 24 patients with

(1) Acta chir scandinav 109 106 115, 1955

Banti's syndrome, aged 6 months to 10 years at the time of surgery. The signs and symptoms of the syndrome, which is due to increase of pressure in the portal circulation, are splenomegaly, pancytopenia and gastrointestinal hemorrhage. Most adult cases are due to cirrhosis of the liver, whereas in children an extrahepatic lesion is usually the cause, e.g., thrombosis of the portal vein or its branches due to infection or trauma, extraportal pressure due to adhesions following peritonitis, enlarged lymph nodes or tumors and biliary calculi, congenital stenosis or atresia of the portal vein and cavernomatous degeneration. It is often difficult to determine the cause of the obstruction of the portal vein at surgery. The site of obstruction determines the signs and symptoms. Measurement of portal pressure during operation, readily accomplished with an ordinary water manometer, may show it to be double or triple the normal pressure of 60-150 mm H<sub>2</sub>O. The collateral veins then swell into large cords of veins by way of which the increased pressure tends to equalize itself into the caval system. The submucosal collateral veins of the stomach and the esophagus can bleed.

The main symptom is hematemesis and the commonest cause of death is hemorrhage. Many patients show lassitude, anemia and general debility. Findings include splenomegaly, anemia, leukopenia and thrombocytopenia due to hypersplenism. In extrahepatic portal hypertension, reactions to liver function tests are normal. Liver biopsies are important in adults with cirrhosis.

Splenectomy was performed as a primary measure in 15 patients (in 2 ligation of the splenic artery was first done). Of these, eight had survived without subsequent treatment for one to seven years. In three, recurrent hemorrhage led to immediate death and in four further operations were performed for bleeding. One of these patients died of recurring hemorrhage after gastrectomy, while three, on whom esophagotomy and ligation of the varices had been performed, were alive and asymptomatic six months to two years later. Splenorenal anastomosis in connection with splenectomy was performed as a primary measure in eight patients. Of these, four were alive and asymptomatic six months to three years later. Hemorrhage recurred in four, of whom two died and two were alive two to seven months

after esophagotomy and ligation of the varices. One patient died in shock during an attempt at ligation of the splenic artery. In all, 7 of the 24 patients died, all of hemorrhage.

Venous anastomosis with splenectomy is the treatment of choice in all patients with hemorrhage due to increased portal pressure. The prognosis following splenectomy alone, however, has not proved wholly unsatisfactory. In recurrent hemorrhages, ligation by esophagotomy has given the best results.

**Surgery of the Spleen** is discussed by A. G. R. Lowdon<sup>2</sup> (Univ. of Durham). Important features of surgical anatomy are profuse blood supply and the fact that vessels reach and leave the hilus through two mesenteries (dorsal mesogastrium) which constitute the limits of the lesser peritoneal sac on the left side, the lienorenal ligament behind and the gastrosplenic ligament in front. Close relation of the tail of the pancreas to the splenic hilus and possible existence of accessory spleens are also important. Accessory spleens are present in about 25% of children and 11% of adults but appear commoner with splenic enlargement. More than half occur at the hilus of the true spleen, but they may be found in gastrocolic, gastrosplenic or splenocolic peritoneal folds, the greater omentum, the mesentery of transverse colon or in relation to splenic vessels and the pancreas. A few occur in less accessible sites, e.g., the mesentery of the small intestine, the region of the left gonad or the mediastinum.

**PROCEDURE**—Splenectomy is usually performed through a left paramedian transverse or subcostal abdominal incision. Transverse incision is advantageous in hemolytic anemia because the biliary tract must be explored. In congestive splenomegaly, the spleen may be adherent to the diaphragm and the posterior part of the lienorenal ligament may contain dangerously large collateral veins. If such difficulties are foreseen a thoracoabdominal exposure through the eighth interspace and epigastrium permits deliberate hemostasis under vision of the abnormal venous collaterals. Opening of the gastrosplenic ligament to expose the main vascular pedicle should be extended to include division of the splenocolic fold of peritoneum, to mobilize the lower pole of the spleen. If the splenic artery is exposed it may be ligated in continuity. The convex surface is then separated from the diaphragm. With the spleen rotated forward and right the posterior peritoneal layer of the lienorenal ligament is divided by a long handled knife or scissors. Mobilization is completed by blunt dissection, lifting the tail of the pancreas forward with the main vascular pedicle. After division of the rest of the gas



Banti's syndrome, aged 6 months to 10 years at the time of surgery. The signs and symptoms of the syndrome, which is due to increase of pressure in the portal circulation, are splenomegaly, pancytopenia and gastrointestinal hemorrhage. Most adult cases are due to cirrhosis of the liver, whereas in children an extrahepatic lesion is usually the cause, e.g., thrombosis of the portal vein or its branches due to infection or trauma, extraportal pressure due to adhesions following peritonitis, enlarged lymph nodes or tumors and biliary calculi, congenital stenosis or atresia of the portal vein and cavernomatous degeneration. It is often difficult to determine the cause of the obstruction of the portal vein at surgery. The site of obstruction determines the signs and symptoms. Measurement of portal pressure during operation, readily accomplished with an ordinary water manometer, may show it to be double or triple the normal pressure of 60-150 mm H<sub>2</sub>O. The collateral veins then swell into large cords of veins by way of which the increased pressure tends to equalize itself into the caval system. The submucosal collateral veins of the stomach and the esophagus can bleed.

The main symptom is hematemesis and the commonest cause of death is hemorrhage. Many patients show lassitude, anemia and general debility. Findings include splenomegaly, anemia, leukopenia and thrombocytopenia due to hypersplenism. In extrahepatic portal hypertension, reactions to liver function tests are normal. Liver biopsies are important in adults with cirrhosis.

Splenectomy was performed as a primary measure in 15 patients (in 2 ligation of the splenic artery was first done). Of these eight had survived without subsequent treatment for one to seven years. In three, recurrent hemorrhage led to immediate death and in four further operations were performed for bleeding. One of these patients died of recurring hemorrhage after gastrectomy while three on whom esophagotomy and ligation of the varices had been performed were alive and asymptomatic six months to two years later. Splenorenal anastomosis in connection with splenectomy was performed as a primary measure in eight patients. Of these four were alive and asymptomatic six months to three years later. Hemorrhage recurred in four, of whom two died and two were alive two to seven months

after esophagotomy and ligation of the varices. One patient died in shock during an attempt at ligation of the splenic artery. In all, 7 of the 24 patients died, all of hemorrhage.

Venous anastomosis with splenectomy is the treatment of choice in all patients with hemorrhage due to increased portal pressure. The prognosis following splenectomy alone, however, has not proved wholly unsatisfactory. In recurrent hemorrhages, ligation by esophagotomy has given the best results.

**Surgery of the Spleen** is discussed by A. G. R. Lowdon<sup>2</sup> (Univ. of Durham). Important features of surgical anatomy are profuse blood supply and the fact that vessels reach and leave the hilus through two mesenteries (dorsal mesogastrium) which constitute the limits of the lesser peritoneal sac on the left side, the lienorenal ligament behind and the gastrosplenic ligament in front. Close relation of the tail of the pancreas to the splenic hilus and possible existence of accessory spleens are also important. Accessory spleens are present in about 25% of children and 11% of adults but appear commoner with splenic enlargement. More than half occur at the hilus of the true spleen, but they may be found in gastrocolic, gastrosplenic or splenocolic peritoneal folds, the greater omentum, the mesentery of transverse colon or in relation to splenic vessels and the pancreas. A few occur in less accessible sites, e.g., the mesentery of the small intestine, the region of the left gonad or the mediastinum.

**PROCEDURE.**—Splenectomy is usually performed through a left paramedian, transverse or subcostal abdominal incision. Transverse incision is advantageous in hemolytic anemia because the biliary tract must be explored. In congestive splenomegaly, the spleen may be adherent to the diaphragm, and the posterior part of the lienorenal ligament may contain dangerously large collateral veins. If such difficulties are foreseen, a thoracoabdominal exposure through the eighth interspace and epigastrium permits deliberate hemostasis under vision of the abnormal venous collaterals. Opening of the gastrosplenic ligament to expose the main vascular pedicle should be extended to include division of the splenocolic fold of peritoneum, to mobilize the lower pole of the spleen. If the splenic artery is exposed, it may be ligated in continuity. The convex surface is then separated from the diaphragm. With the spleen rotated forward and right, the posterior peritoneal layer of the lienorenal ligament is divided by a long-handled knife or scissors. Mobilization is completed by blunt dissection, lifting the tail of the pancreas forward with the main vascular pedicle. After division of the rest of the gas-

(2) Ann Roy. Coll. Surgeons England 16:400-411, June, 1955.

trosplenic omentum with the vasa brevia the spleen can be lifted exposing the main vascular pedicle at the hilus for dissection. The artery is ligated first and the spleen made to contract before the vein is closed. Main vessels should be doubly ligated.

In hemolytic anemia or thrombocytopenic purpura careful search must be made for accessory spleens, which must be removed. In hemolytic anemia, the biliary tract is examined for pigment stones. The edge of the gastrosplenic omentum may be sutured to the parietal peritoneum in the splenic bed, but reconstruction of the left side of the lesser sac is not necessary. Drainage is not required unless the pancreas has been injured or hemostasis is unsatisfactory. If platelet count rises over 1 000,000 during the first week after operation heparin should be given until the count falls as protection against possible portal thrombosis which is likely to be rapidly fatal unless the patient has a well developed collateral circulation.

After splenectomy, red cell destruction diminishes, and red cells become thinner and less fragile. Reticulocytes increase, and erythrocytes may contain nuclear fragments (Howell-Jolly bodies). Red blood cell count in peripheral blood falls at first but returns to normal in three to four months. Lymphocyte and platelet counts rise but later return to normal. None of these changes is significant in absence of previous functional derangement. There is no evidence that an adult without a spleen has any reduction of exercise tolerance or of resistance to bacterial infection. A man, aged over 70 who had lived a healthy life for 56 years after splenectomy for traumatic rupture, had a massive hematemesis from gastric ulcer. He tolerated emergency partial gastrectomy as well as many a younger man with a spleen. Experience suggests that the spleen plays a more important part in resistance to infections in children than in adults, and splenectomy should, if possible, be avoided in infancy.

**Surgery in Patients with Hemorrhagic Tendency** According to J. P. Soulier<sup>3</sup> (Paris), splenectomy, the only operation indicated in thrombopenic purpura, should be performed in all cases in which idiopathic thrombopenia persists over a year, with frequent hemorrhages requiring transfusions. Intervention is indicated oftener in adults than in children and in women than in men. Absolute contraindications are marrow depletion with megakaryocytic aplasia or malignant hemopathy. Relative contraindications are acute thrombopenia (first attack) or thrombopenia second

ary to infection or drug therapy, because the patient may recover without splenectomy, the condition may recur despite splenectomy, and operation during the acute phase carries a high mortality (about 30% instead of 5%). Nevertheless emergency splenectomy may be justified when hemorrhage is not controlled by transfusions.

In chronic cases splenectomy should be performed after a hemorrhagic episode, in women, during the postmenstrual period. Before operation, anemia should be corrected by isogroup transfusions. Transfusions should not be given the morning of operation, but blood lost during operation should be replaced. Generally, splenectomy is easy, but careful search must be made for accessory spleens, these are especially frequent in children.

Cortisone is useful in acute cases before emergency splenectomy but is unnecessary when operation is performed during a nonhemorrhagic phase in chronic cases. Therapeutic trial with cortisone or hydrocortisone should be carried out with the hope of avoiding splenectomy. Cortisone should not be discontinued suddenly in a patient to be operated on. Operation should be performed two or three weeks after an ineffective course of cortisone or while the patient is taking cortisone. Doses should be reduced gradually during the postoperative period. If cortisone is to be effective its maximal effect should be evident about the fourth day. Failure with cortisone is an indication for splenectomy and patients failing to respond to splenectomy are treated with cortisone. About 5% of patients do not respond to either surgical or medical treatment and must receive repeated blood transfusions.

In about 75-80% platelets return to normal after splenectomy and the patient is permanently cured. In about 5-10%, thrombopenia recurs though often with decreased hemorrhages. Failure is sometimes due to accessory spleens and reoperation is often successful. Failure to respond to splenectomy cannot be predicted preoperatively. Despite modern transfusion techniques and cortisone immediate mortality in emergency splenectomy reaches 20-30%, but late results are comparable to those in chronic cases. In children spontaneous recurrences are frequent (73% in a Mayo Clinic series). Operation should be deferred until puberty, being

used principally in girls who have metrorrhagias requiring transfusions

In hemophiliacs, surgery is reserved mainly for serious joint disturbances from hemarthroses, with marked functional impairment that does not respond to physical therapy. Such operations entail great risk, especially from late massive hemorrhages and infections. Minor surgery is as dangerous in hemophilia as major procedures. The gravity of certain hemorrhagic complications justifies operation—e.g., tarsorrhaphy in retro orbital hematoma, subaponeurotic hematoma causing paralysis or ischemia of an extremity, and hemothorax. When surgery is decided on, the coagulation defect must be corrected before operation with blood, plasma or a plasma fraction containing the antihemolytic factor. Transfusions should be administered immediately before operation, not several hours previously. Hemorrhage is likely to occur two to seven hours after operation, late hemorrhages are more serious than early ones and are difficult to prevent. Postoperative transfusions are given daily for eight days and then less often.

Surgery is contraindicated completely in refractory hemophilia or in the presence of a circulating anticoagulant. In conditions related to classic hemophilia, in which there is a defect of fibrinogen, prothrombin, proconvertin or proaccelerin (parahemophilia), surgical problems are essentially the same. In patients with prolonged clotting time (Willebrand's syndrome, thrombopathy), preoperative treatment with cortisone or ACTH is effective in controlling surgical hemorrhage.

---

## THE BILIARY TRACT

Excretion of Erythromycin through Biliary Tract following intravenous administration was studied in eight patients by Y. Takimura and M. Lopez Belio<sup>4</sup> (Chicago Municipal Tuberculosis Sanitarium). Six had had cholecystectomy 10-14 days previously and two had no hepatic or biliary disease. Erythromycin given intravenously was concentrated in the liver and excreted in bile in high concentrations in patients

after cholecystectomy. Those showing varying degrees of jaundice had higher erythromycin serum concentration than normal subjects. Erythromycin was seen initially in high concentration in duodenal aspirates from patients without hepatic or biliary tract disease, but drug concentrations declined more rapidly in duodenal aspirates than in common duct bile though total amount recovered in the former specimens was about three times greater than in the latter. Drug excretion in urine was slightly higher for jaundiced than nonjaundiced patients. Excretion and concentration of erythromycin in gastric aspirate from one patient with T tube drainage were negligible compared with those in bile.

Reliability of Cholecystography was evaluated by Ingmar G. Wickbom and Uno Rentzhog<sup>5</sup> (Stockholm) in a study of 1,340 patients with abnormal cholecystograms subjected to operations. In 552, the only contrast medium used was cholotrast, and in 788 bilitrast or both. Lack of filling was the most common abnormality (56%) and the only one in 45%. The gallbladder filled in 48% of cases in which bilitrast was used, but only in 38% with cholotrast. With bilitrast, filling occurred in 23% and, with cholotrast, in 17% of cases with thickening of the wall. When gallbladder walls were normal, filling occurred in 74% with bilitrast and 67% with cholotrast. These differences are statistically significant. In 21 of 35 cases with no filling and no stones, the wall was so changed that filling was impossible with any contrast medium. The gallbladder was normal in 21 of 25 cases in which operation was performed despite an apparently normal cholecystogram. Three of these patients were paratyphoid carriers. In four, two from the cholotrast and two from the bilitrast series, stones were found. Operation disclosed a stone in the common duct in 10.9% of the entire series, in 5.1% with filling of the gallbladder and stones and in 15.5% in which the gallbladder failed to fill.

Whenever cholecystography points to gallstones, either directly or indirectly as defects in its contrast-filled lumen, the evidence may be relied on almost completely. Failure of the gallbladder to fill is almost conclusive evidence that it is diseased, provided correct technic, especially in ingestion of the medium, is used, and the patient has had no vomiting or diarrhea afterward. The walls were diseased in three fourths

(5) Acta radiol 44 185 200, September, 1955

of cases in which the gallbladder failed to fill but in only one fourth in which stones were visible in a contrast-filled gallbladder. When the gallbladder fails to fill, extensive injury to liver parenchyma must be excluded. Other sources of error are retention of contrast medium in the stomach, pernicious anemia and breast feeding, and local lesions such as tumors of the gallbladder, biliary ducts or head of the pancreas, and duodenal ulcer, which may cause defective filling. Bilitrast is more likely than cholotrast to lead to filling of the gallbladder, whether or not its walls are diseased, hence there is a better chance of direct visualization of stones with bilitrast. A normal cholecystogram practically always excludes disease of the gallbladder, although rare exceptions do occur.

► [In the 32 years that have elapsed since we published our first article on cholecystography there have been many changes in the contrast material but practically no change in the interpretation. This turn of events was predicted by us. There is no assurance that even now the most ideal substance has been found. It is gratifying to know that the principles of interpretation laid down by us in 1924 still hold true and that this method of examination continues to be important in establishing the diagnosis of cholecystitis and cholelithiasis. On the other hand it is curious and somewhat inexplicable that many roentgenologists speak of the 'filling and failure to fill' of the gallbladder. What is meant of course is visualization or nonvisualization of the organ and that is very different. In nearly all instances the failure to become visualized is due to disease of the gallbladder, usually with thickening of its wall so that water is not absorbed sufficiently to concentrate the contrast medium enough to give a shadow. That phenomenon has nothing to do with filling. Rather it is evidence of whether or not the function of the organ is normal.—Ed.]

**Cholecystographic Studies during and Immediately Following Acute Pancreatitis** are reported by Van G Kaden, John M Howard and Leonard C Doubleday<sup>6</sup> (Baylor Univ.). Among 23 patients during the first week of convalescence from acute pancreatitis, the gallbladder was not visualized in 11 and impaired function was indicated in 4 others (total 65%). Cholecystograms during follow-up studies or surgical exploration indicated that these patients had no organic disease of the gallbladder. Return of cholecystic function, as indicated by cholecystography, characteristically occurred within a month after symptoms of acute pancreatitis had subsided.

These findings indicate that during the first week of illness with acute pancreatitis a cholecystogram is of diagnostic assistance only if the gallbladder is visualized, for

nonvisualization at this time does not necessarily indicate organic cholecystic disease

Studies of battle casualties showing nonvisualization following severe injury of any type would strongly suggest that this phenomenon is not specific for direct pancreatic injury. Since intravenous administration of cholecystographic medium may also result in nonvisualization, failure of intestinal absorption of the medium is not the only defect. Paralytic ileus of the gallbladder with failure of intermittent emptying and refilling might be postulated as the basic underlying difficulty. Diminution in absorption of water by the gallbladder may prove to be a factor.

**Intravenous Cholangiography: Results in 100 Cholecystectomized Patients with Upper Abdominal Symptoms** David J. Sandweiss and Harold Fulton<sup>7</sup> (Harper Hosp., Detroit) used sodium iodipamide (cholografin®) to perform intravenous cholangiography in 100 patients with mild to severe epigastric and/or right upper quadrant symptoms that represented or suggested biliary tract disease. The common duct and hepatic radicles were visualized in 94. Excluding duplication, 34 had normal cholangiograms (Fig 91), 7 stones in the common ducts (Fig 92) and 3 dilated cystic duct stumps or "reformed" gallbladders. Thus in these 44 patients the cholangiographic findings were clearly normal or abnormal and were of distinct value, despite the fact that the incidence of false negative cholangiograms is not known.

Moderate to marked dilatation of the common ducts (Fig 93), found in 30 patients, was unassociated with stones in the cholangiograms in 25, and 24 had common ducts of normal width without apparent stones but with the terminal ends of the ducts not visualized. In these 49 patients the results were equivocal. In one patient with a dilated common duct, a stone was suspected and though not found at one exploration was found at second exploration. Four of the patients with dilatation of the ducts had definite stones in the cholangiograms. Of 64 with ducts considered to be of normal width, 3 had stones.

The significance of dilatation of the common duct without apparent stones is not clear, though some of these patients might have had stones not visualized on intravenous



cholangiography. It appears that the width of the common duct as measured on the x-rays depends neither on the presence or absence of visualized stones nor on the interval of time between cholecystectomy and cholangiographic study.



Fig. 91 (above left)—Intra-venous cholangiogram showing normal sized (4 mm) common duct.

Fig. 92 (above)—Cholangiogram showing common duct of normal width (6 mm) that contains two calculi (arrows). Two small black objects to left of duct represent actual calculi.

Fig. 93 (left)—Cholangiogram showing dilated common duct (14 mm wide). Terminal end of duct is not visualized. Upper arrow indicates cystic duct stump.

(Courtesy of Sandweiss D. J. and Fulton H. J. *AMA* 159:998-1001, No. 5, 1955.)

The common duct does not necessarily dilate as a compensatory mechanism after removal of the gallbladder.

Intravenous cholangiography has some important limitations. Bile duct visualization apparently fails in patients with jaundice as well as in nonicteric patients with impaired liver function. In 44% of the patients in this series, the

terminal end of the common duct, a critical area, was not visualized

**Evaluation of Early Operation in Acute Inflammation of Gallbladder** was made by Patrick C Shea, Jr.<sup>8</sup> Of 209 patients undergoing cholecystectomy in a three year period at the Grady Memorial Hospital, Atlanta, Ga., 51 were operated on within 24 hours of admission and during the acute period of the disease and 158 were first treated conservatively and later had elective surgery. Early operation is advisable for those who give the clinical impression of impending gangrene or perforation and for those with severe manifestations of acute cholecystitis, either static or progressive, whose general health is excellent. Management with antibiotics, supportive therapy and ultimate elective surgery are advisable for those whose symptoms are subsiding and whose general health makes elective operation the wiser procedure. Elective surgery is used in patients with chronic cholecystitis.

The 51 patients subjected to immediate surgery were observed a minimum of four to six hours while diagnostic tests and evaluation of hydration were performed. Fluids and blood were given as indicated and nasogastric suction was instituted. Narcotics were withheld. Antibiotics were used in patients with signs of peritonitis. Early operation was indicated in patients who had progressive and rebound tenderness over the gallbladder region continued or heightened fever, persistent, elevated white blood cell count and constant or increasingly severe pain. During surgery, the cystic duct or artery was not touched with instruments.

Of the 209 patients 149 were white and 60 were Negroes. The Negroes were younger than the whites and the men younger than the women. Those operated on early were older than those treated conservatively. A history of one or more previous attacks was found in 63.5% of those operated on early.

Pathologic findings were acute cholecystitis in 12, acute and chronic cholecystitis in 57, chronic cholecystitis in 135, autolyzed containing stones in 3 and carcinoma in 2. Among the 51 patients with early cholecystectomies, the diagnosis of acute or acute and chronic cholecystitis was made in 82%.

The over all mortality rate was 2.9% in those operated

on early it was 59% and in those operated on electively 19% Mortality rate without common duct exploration was 16% and with common duct exploration, 15.8% Most patients, even when recovery was uncomplicated, had fever after operation Postoperative complications, in many instances multiple, occurred in 14% of the elective group and in 37% of the immediate surgery group It was found that 85% of the patients with infected cholecystectomy wounds were diabetics There was no evidence of common duct stricture or any other type ductal damage in the series A definite postcholecystectomy syndrome was found in six patients, five of whom had elective operations This was in the ratio of 32% for the elective patients to 19% for those with early operation

The study shows that mortality and incidence of complications are greater among patients with early cholecystectomy The best time to operate is four to six weeks after acute symptoms have subsided When early intervention is indicated, it is best to operate no later than five to seven days after onset of the acute attack, and preferably within four days The indications for exploration of the common bile duct should be conservative to prevent complications

► [Interesting to see the swinging of the pendulum Until about 20 years ago with rare exceptions it was not considered good practice to operate in cases of acute cholecystitis largely for the reasons that Shea mentions in his article Can it be that the younger surgeons are now learning those truths?—Ed]

**Study of Serum Amylase Concentration in Patients with Acute Cholecystitis**, made by Emmett R Hall Jr, John M Howard, George L Jordan, Jr, and Raymond Witt<sup>9</sup> (Baylor Univ) included 75 subjects Normal range was established in 70 controls as 15.50 units/100 ml Serum amylase concentration was elevated in seven patients (68-128 units) and two others had concentrations between 50 and 60 units All with high amylase levels had stones in the biliary tree as did 92% of the entire series Three of the patients with elevated concentrations had mild to moderate pancreatitis at operation in the others no abnormality other than acute cholecystitis was noted Complete pancreatic exploration, however, was not performed

The mechanism by which serum amylase concentration becomes elevated in patients without gross pancreatic dis-

(9) Ann Surg 143:517-519 April 1956

case is speculative. It is possible, although not proved, that it is due to temporary spasm of Oddi's sphincter, resulting in obstruction of pancreatic outflow. An elevated serum amylase concentration is not pathognomonic of primary acute pancreatitis, and this finding alone is not evidence enough to alter the treatment of acute cholecystitis.

Clinical Pathology of Papilla of Vater is important, according to W. Hess<sup>1</sup> (Univ. of Basel), in planning adequate treatment of biliary tract infections. Increased insight into pathology of this organ has resulted from operative cholangiography.

Cholangiographic study has demonstrated the striking frequency of inflammatory stenosis of the papilla as a complication of cholelithiasis. Papillitis is present in about 33% of cases with cholelithiasis and in about 59% of cases with choledochal stones. Even when stones are absent, papillary stenosis may cause dilatation of the duct, ascending cholangitis, icterus and colic. If the pancreatic duct is also stenosed, chronic pancreatitis may develop. If stenosing papillitis is overlooked at operation, postoperative colic and icterus occur. Secondary operations after cholecystectomy reveal papillitis in 40%. Clinically, symptoms of unrecognized papillitis cannot be distinguished from those of choledochal stone, i.e., icterus, colic, increased alkaline phosphatase level and cholangitis.

Most cases of papillitis occur with cholelithiasis, especially choledochal stones, but the papilla may be primarily diseased, with no stones or other lesions in the biliary tract. Recognition of papillitis (primary or secondary) is important because these cases formerly were classified as surgical failures. When operation is performed for choledochal stone and no stone is found, it is assumed that it has "disappeared," and a normal gallbladder is removed as a presumed source of lithiasis, or the abdomen is closed after exploration because of "mistaken diagnosis." In either case, the papillitis which caused the colic remains untreated, and symptoms recur. Proper treatment of primary papillitis consists in sphincterotomy and transpapillary T drainage. A healthy gallbladder does not need to be removed, because it regains its function after sphincterotomy.

About 50% of cases of chronic recurring pancreatitis are

(1) Schweiz. med. Wchnschr. 85:493-496 May 21, 1955

caused by papillary stenosis causing obstruction of outflow of pancreatic juice. Obviously these cases are not treated satisfactorily by the usual cholecystectomy or even by choledochoduodenostomy. Incision of the papilla often is necessary to restore pancreatic flow.

With manometric cholangiography, changes in tonus of Oddi's sphincter, whether hypo- or hypertonic, can easily be recognized. With hypotonia, resistance of the sphincter falls to less than 10 cm water and x-ray shows a gaping papilla. With hypertonia, the sphincter shows contraction (spindle shaped), the cystic duct and whole choledochal tract may also be contracted, with biliary tract pressure increased to over 15 cm water. Lithiasis is often present in these cases. Hypotonia of Oddi's sphincter is a frequent sequel of acute inflammatory diseases, gallbladder empyemas, acute pancreatitis and functional prolapse of the gallbladder. Hypertonia is a sign of vagotony and is often found with duodenal ulcer.

Benign tumors of the papilla of Vater are rare but may be a cause of biliary tract obstruction. Papillary carcinoma can be well visualized by cholangiography. This is important, because radical removal results in about 30% of five year cures, whereas in carcinoma of the head of the pancreas, which causes similar symptoms, prognosis is so grave that radical operation is not justified.

**Unsatisfactory Results after Cholecystectomy**, according to S. H. Lovell<sup>2</sup> (Sydney), are most often due to poor selection of patients for operation. Difficulties are more likely to arise in patients who have not had real pain, but had flatulent dyspepsia, nausea and biliousness or migraine. The most common type of unsatisfactory result is the so called postcholecystectomy syndrome.

Postcholecystectomy syndrome occurs more often when no stones are found in the removed gallbladder, results are disappointing in about 65% of such cases. Many patients who appear initially to have gallbladder disease would, on more prolonged assessment be found to have some other lesion, such as peptic ulcer, hypertrophic gastritis, hiatus hernia, chronic hepatitis, coronary disease, renal or colonic disease or even appendicitis. The most common finding at laparotomy for this syndrome is dense adhesion of the

pyloroduodenal segment to the region of the gallbladder fossa. Lovell recommends separating these adhesions carefully, securing as complete hemostasis as possible, and placing some omentum between the pyloroduodenal segment and the liver. Residual stone in the common bile duct is rarely found. Infrequency of jaundice in the postcholecystectomy syndrome is striking.

Aside from instances of erroneous judgment and a small group in which an incorrect diagnosis has been made, a still smaller group shows some other cause for postcholecystectomy syndrome, including residual stone in the common bile duct, residual remnant of the gallbladder or bulbous cystic duct, with or without stone, stricture of the common or hepatic duct, neuroma of common duct stump, stricture of ampulla of Vater, chronic pancreatitis, and retained foreign bodies. It should be remembered also that the gallbladder may be present despite the patient's belief that it has previously been removed.

Cases of postcholecystectomy syndrome require detailed study. Valuable assistance may be obtained at times with intravenous cholangiography, but results must be interpreted cautiously, and alarming anaphylactic reactions have occurred. When exploratory laparotomy is advisable, it should include a full examination, with careful separation of adhesions and, with few exceptions, a thorough exploration of the common bile duct. In a few patients, relief may follow vagotomy and in others exhibition of pro banthine® will be helpful. Some have obtained relief from preparations of pancreas and others from luteal hormones or through histamine desensitization. There will remain a group in which all treatment fails.

**Postcholecystectomy Syndrome.** Eric Samuel<sup>3</sup> (Johannesburg) studied 36 patients with abdominal symptoms by intravenous cholangiography. The patients were given 40 cc biligrafin intravenously, and films were taken at 15 and 40 minutes in prone and prone oblique positions. Tomograms taken in the prone right oblique or prone oblique positions visualized the common bile duct more clearly than routine views.

Symptoms included severe colicky pain localized to the right hypochondrium, sometimes radiating through to the

back, or not colicky and not radiating, distention and flatulence, often associated with biliousness, jaundice, elevated temperature and indigestion

Radiologically, the patients were divided into three groups (1) those with normal extrahepatic biliary system, (2) those with common bile duct stones, stones in the cystic duct or strictures of the bile ducts, and (3) those with dilatation of the common hepatic duct and common duct without any demonstrable cause. Stones in the common bile duct, or in the fragment of cystic duct remaining, were found in eight patients, most of whom had colicky pain. Postoperative stricture of the bile duct was found in one. Remnants of the cystic duct were found in eight and from the size and dilatation of the remnant, three were judged responsible for the symptoms. Only three patients showed marked dilatation of the common bile duct without obvious causes. As the contrast medium did not enter the duodenum for a considerable period, dilatation was probably due to some obstruction at the sphincter of Oddi. Dilatation of the common bile duct was not an invariable postoperative finding, and there is considerable doubt whether postoperative dilatation is a compensatory mechanism. The inhalation of amyl and octyl nitrite did not affect radiographic appearance of the dilated ducts. Infection and pancreatitis may play a role in postoperative dilatation of the bile ducts.

**Postcholecystectomy Dyskinesia With Pancreatitis, Sphincteritis and Choledocholithiasis as Causes** Waltman Walters<sup>4</sup> (Mayo Clinic and Found.) reports that the most frequent causes of pain recurring after cholecystectomy, especially if stones were present in the gallbladder, are overlooked stones in the common duct, stricture of the bile ducts, a remnant of gallbladder, with or without stones, an elongated cystic duct that is inflamed or contains stones, malfunction of the sphincter of Oddi, pancreatitis, intra-abdominal lesions, usually obstructive or perforative, such as duodenal ulcer, inflammatory lesion of the intestine and intra abdominal carcinoma and retroperitoneal lesions, involving such structures as the right kidney and the right adrenal gland and including retroperitoneal lymphoma and sarcoma.

It may be difficult to localize the lesion, and abdominal

exploration is often necessary, even after carefully elicited history, physical examination and judicious use of laboratory procedures, including x-rays with sodium iodipamide (cholografin<sup>\*</sup>). Exploration includes the interior of the common and hepatic ducts, the pancreas, duodenum, sphincter of Oddi and the entire gastrointestinal tract and retroperitoneal region.

Patients without jaundice and without a stone in the common or hepatic duct present a difficult diagnostic problem. Jaundice simplifies diagnosis because it localizes the lesion to the liver, biliary passages and pancreatic regions. Dysfunction of the sphincter of Oddi, with or without pancreatitis and with or without cholangitis, is difficult to evaluate. Sphincterotomy or choledochoduodenostomy, or both, has been performed with varying degrees of success. The relief from symptoms may be complete or partial, i.e., less pain and lowered frequency. What procedure to perform depends on whether there is enlargement of the head of the pancreas, due to inflammation, narrowing of the pancreatic portion of the common bile duct with biliary stasis or dilatation of the common duct.

External drainage of the common duct with a T tube kept in for a prolonged period has been used in the past. Recently internal drainage by anastomosing an opening in the common duct to an opening in the duodenum has been performed. If the common duct is small and there is uncertainty as to whether the lesion is pancreatitis or dysfunction of the sphincter of Oddi, transduodenal sphincterotomy has been performed. An effort must be made to find the main pancreatic duct in the ampulla and to catheterize it. Some patients have a narrowing in the part of the duct not too far distant from its opening in the ampulla, whereas others have no obstruction.

Some patients with no relief from symptoms after prolonged T tube drainage, choledochoduodenostomy and sphincterotomy have benefited from splanchnic nerve block with alcohol or from splanchnicectomy. One patient had complete relief after chordotomy.

**Bile Drainage after Choledochostomy in Man, with Some Observations on Biliary Fistula.** F. F. Rundle, M. H. Cass, B. Robson and Margaret Middleton<sup>5</sup> (Sydney) studied the

(5) *Surgery* 37 903 910, June, 1955



bile drainage after 27 operations for choledochostomy in 25 patients who had common duct drainage through either a T tube or a cuffed Foley catheter. In all patients but one, the gallbladder was either removed or functionless. The secretion of bile immediately after choledochostomy is considerably depressed, and recovery occurs only gradually during the first one to two weeks after operation. Immediately postoperatively the daily bile drainage averaged 250 cc, rising gradually to about 500 cc 15 days later. The 24 hour drainage ranged from 20 to 1,060 cc. The average volume from the tenth day onward, when the flow leveled off, was  $478 \pm 186$  cc/24 hours. The hepatic secretion of bile was found to be continuous and not subject to diurnal variation. The increase of bile drainage a few days postoperatively was independent of the food intake. The immediate postoperative bile drainage depression is probably due to true functional depression of the liver. Prolonged exposure of the liver to air at room temperature, intra abdominal manipulations, including handling and retraction of the liver, and the impact of anesthetic agents might be factors in this depression.

There was little difference between the amount of drainage through the T tube and the cuffed Foley catheter. Drainage of the bile through a T tube in the common duct is virtually complete, provided its vertical limb remains unobstructed. Practically total loss of bile through a biliary fistula may persist for long periods in the absence of obstruction at the lower end of the common duct.

Dilatation of the duct system at operation was associated with an increase in daily flow of bile. The explanation for this is unknown. It may be due to increased obstruction or to increased duct surface.

**Strictures of Bile Ducts and Their Treatment** James A. Boren and Waltman Walters<sup>6</sup> reviewed 88 procedures performed on 81 patients from January 1952 through June 1954. Among 77 patients with previous cholecystectomy, the common duct stricture was due to operative trauma in 73 and to inflammation or overlooked common duct stones, in 4. Among the four without previous cholecystectomy, the stricture was due to trauma during gastric resection in two and to nonpenetrating external trauma to the abdomen, re-

sulting in bile peritonitis requiring drainage, in two. A biliary fistula was present in 67% and was often accompanied by bile peritonitis. Jaundice was the commonest sign of injury to the common duct and was present in 84% though often it did not appear until a biliary fistula closed. Jaundice appeared weeks to 15 years after cholecystectomy. Eight patients with no definite evidence in the postoperative period that stricture would develop, had jaundice months after the cholecystectomy. Of the 81 patients, 28 had one previous corrective procedure on the common duct, 14 had two, 1 had three and 1 had four.

All patients with stricture of the common bile duct, no matter how many previous operations they have had, should have re-exploration unless hepatic decompensation with ascites is present. The operations used were anastomosis of hepatic and common bile duct to duodenum (58%), duct-to-duct (23%) duct to jejunum (9%) and external drainage of one or both intrahepatic ducts (9%). At surgery, the dissection should be continued until the ends of the duct, or at least the upper unobstructed portion, is found, even though intrahepatic exploration and drainage are required. Duct-to-duct anastomosis is used when both ends of the duct of sufficient size can be found is more easily accomplished in early stages before the duct distal to the stricture becomes scarred and is usually the procedure of choice in recent damage to the common duct. Anastomosis of duct to jejunum is a lengthier procedure and is generally reserved for use when the duodenum cannot be approximated to a short stump of hepatic duct above the stricture. Hepaticostomy is a palliative procedure performed when the risk of operation is great for a patient with complete stricture of the extrahepatic ducts who is too ill to undergo anastomosis between the intrahepatic ducts and the intestines. Prosthetic splints were used in 79 of the procedures and helped to prevent transient postoperative edema from obstructing the anastomosis and fibrosis from developing during the first few postoperative months.

Operative mortality rate was 4.5%. Of 40 patients having 41 procedures, who were followed 22-34 months, 49% were well, 32% had recurrence of symptoms of biliary obstruction (8 of these had further surgery), 7% were lost to follow-up, 7% died postoperatively and 5% died later. Recur-

rences were noted in patients with repeated episodes of cholangitis, stones in the biliary tree and prolonged bile fistula. Anastomosis of the common duct to the duodenum gave as good results as anastomosis of the hepatic duct to the duodenum.

**What Not to Do in Gallbladder Surgery** is suggested by Heneage Ogilvie<sup>7</sup> (London, England). The operation should never be regarded as an emergency, for the disasters of biliary surgery are encountered when this advice is neglected. The gallbladder is distensible and can expand 50 fold. In acute cholecystitis, a stone causes a blocking of the cystic duct, partly mechanical and partly inflammatory. When inflammation subsides, as it does in 19 of 20 attacks, bile flow is restored. If infection does not subside, the gallbladder expands to hold inflammatory exudate, and the omentum wraps around to wall it off. An infected gallbladder seldom bursts, and it does not do so early, suddenly or without abundant warning. If the attack does not respond to rest and chemotherapy and if swelling, leukocyte count or pulse rate is mounting, operation must be performed. The gallbladder may have to be removed if it is gangrenous, but usually it is drained and removed safely and easily at an interval operation.

The common duct must never be explored unnecessarily and should be opened only if it contains stones. In doubtful cases, recourse may be had to cholangiography but need for this should not arise more than once or twice a year. Confidence that the common duct does not contain stones may be based on the following points: (1) Though repeated gallstone attacks may have been followed by deep jaundice, there has been no lemon yellow discoloration, with malaise, that indicates lodging of a stone in the common duct. (2) The common duct does not exceed  $\frac{1}{3}$  in in diameter or show the blue color that suggests black contents. (3) Palpation from the hilum to the bile papilla reveals no irregularity. (4) Aspiration with a fine needle draws off only clear yellow bile with no debris or solid flecks. (5) On isolation of the cystic duct before division its diameter is less than that of the stones felt in the gallbladder.

When the common duct has been opened, it should be treated gently. Stones should be removed without trauma,

(7) Canad. M. A. J. 74:13 Jan. 1, 1956

the opening into the duodenum should not be dilated unduly and chemicals should not be introduced unnecessarily. Contrast mediums are irritating, and their use should not be necessary in more than 1 operation in 50. Stenosing chole-  
dochitis is seldom seen in one who has not been operated on and uncommonly in one in whom the duct has not been opened. It seems in some way to be related to trauma of exploration and possibly to injection of chemicals, particularly of ether. Papillary stenosis is possibly related to stenosing chole-  
dochitis and is seldom seen except when the common duct has been explored. It probably results from forcible dilatation and rupture of fibers of the sphincter of Oddi. The papilla should never be dilated to more than 7 mm., and Oddi's sphincter should never be cut except under direct vision.

Diathermy should never be used inside the abdomen and never on the gallbladder, the gallbladder bed or the liver. There is no finer culture medium for bacteria than cooked liver. A gallbladder bridge or pillow should never be used, for, while it brings the duct region forward, it increases tension of the anterior abdominal wall and hyperextends the spine, leading to shock at the time and permanent backache afterward.

Report on Surgery of Biliary System and Pancreas for 1954 is presented by George A. Hallenbeck, Waltman Walters, Howard K. Gray, James T. Priestley and John M. Waugh.<sup>8</sup> Cholecystectomy was done in 59 of 65 patients with acute cholecystitis; 17 of the 59 also had exploratory choledochostomy, and stones were recovered from the common bile ducts in 6. Cholecystostomy was done in six patients. No hospital deaths occurred after these operations. Of 1,036 patients operated on for chronic cholecystitis, 962 (93%) had gallstones; cholecystectomy alone was done in 769, cholecystectomy with exploration of the common bile duct in 246 (23.7%), with recovery of stones in 95 (38.6%). Indications for exploration of the common bile duct were history of jaundice or of chills and fever, presence of palpable stones, enlargement of the common bile duct and presence of small gallstones in the gallbladder, with a large cystic duct. Hospital mortality for the 1,036 patients was 0.7%. Exploration of the common bile

(8) Proc Staff Meet Mayo Clin 30 640 646, Dec 28, 1955

duct without operation on the gallbladder in 55 revealed stones in 24. Use of intravenous cholangiography may increase future accuracy of preoperative diagnosis of choledocholithiasis.

Cholecystectomy was performed in 7 of 10 patients with carcinoma of the gallbladder and choledochostomy in 1, and extent of disease limited operation to exploration in 2. The Whipple operation was performed in three of five patients with carcinoma of the ampulla of Vater, two of whom died postoperatively. A small tumor was excised locally in an elderly woman in poor condition, and palliative choledochoduodenostomy was done to relieve jaundice in the fifth. Only one of nine patients with carcinoma of the bile ducts was suitable for radical resection. Four had exploratory laparotomy alone, and some palliative procedure to relieve jaundice was done in four. Part of the liver was resected in seven patients for metastatic neoplasm, usually with some other operation.

Among 74 patients with benign stricture of the bile ducts, anastomoses were made between (1) the hepatic duct or ducts and the duodenum in 32; (2) the common bile duct and the duodenum in 20 (total of 52, or 70%); (3) the hepatic duct or ducts and the jejunum by Roux Y technic in 7 (9.5%) and (4) portions of the common bile duct in 8 (10.8%). Establishment of an external biliary fistula was all that could be done in six, and a plastic operation was performed in one. No hospital deaths occurred.

Sphincterotomy of Oddi's sphincter was performed in 35 patients with biliary colic after cholecystectomy or with acute pancreatitis if stones could not be found in the common bile duct; 21 had pancreatitis and 14 "biliary dyskinesia," or spasm or stenosis at the ampulla. Of 43 patients with pancreatitis diagnosed at operation, 21 had sphincterotomy. 9 had anastomoses between the biliary tract and intestine, 4 had drainage of the common duct, 3 had partial pancreatectomy and 6 had abdominal exploration. Of seven pseudocysts of the pancreas, two were excised, two were marsupialized and three were anastomosed to the gastrointestinal tract. Partial removal of a constricting ring of pancreatic tissue was done in three patients, and one islet cell tumor was excised. Exploration alone was done in 34 of 76 patients with pancreatic carcinoma.

Palliative procedures for relief of jaundice or duodenal obstruction were performed in 35. The Whipple operation was done in seven without a death. This operation is used by the authors only in treatment of small lesions, without metastases, in carcinoma of the pancreatic head but is employed more aggressively for ampullary carcinoma. Percutaneous needle biopsy of the liver was done 134 times, with one death (0.7%). Biopsy of the liver at exploratory laparotomy was the sole procedure in 28 patients. In two patients hepatic abscesses were drained.

**Primary Carcinoma of Gallbladder** is reported by C Douglas Sawyer and J F Minnis, Jr<sup>9</sup> (Methodist Hosp of Brooklyn). Between January 1939 and December 1953, 1,752 cholecystectomies were performed. Carcinoma of the gallbladder was found in 27 patients, aged 41-88, most of whom were over age 60. Women were more commonly affected than men. Cholelithiasis was present in 25. There are no early symptoms of carcinoma of the gallbladder, those of cholelithiasis usually being the first. Symptoms of acute and chronic cholecystitis were present in 16 patients. Four had history of jaundice, 10 were jaundiced on admission. 5 had weight loss, 7 had a palpable mass in the right upper quadrant, 1 had anemia and 15 had leukocytosis.

X rays were of diagnostic value in 17 of 23 patients. Cholecystograms done in 14 showed nonvisualization in 11 including 1 with radiopaque stones, lithiasis in 2 and poor function without lithiasis in 1. Correct diagnosis was made preoperatively in only 2. Cholecystitis or choledocholithiasis or both was the preoperative diagnosis primarily considered in 20. Primary malignant disease limited to the gallbladder often may not be obvious at laparotomy or during cholecystectomy. Among 24 patients with laparotomy diagnosis was made during surgery in only 14, 5 were considered to have chronic and 5 acute cholecystitis. Adenocarcinoma was found in most patients, squamous carcinoma in only 15%. All patients with epidermoid carcinoma died within six months of hospitalization. Acute cholecystitis was found histologically in 26%.

The only treatment for primary carcinoma of the gallbladder is surgery. Purely palliative or diagnostic sur-

(9) *Am J Surg* 91:99-104, January 1956.

gery was performed in 7 patients, 13 had cholecystectomy and 4 had radical surgery—cholecystectomy with wedge resection of the liver, cholecystectomy and omentectomy, cholecystectomy and wedge resection of the liver, gastrohepatic omentum and regional lymph nodes, and cholecystectomy, transverse colostomy and partial duodenectomy. Over-all operative mortality rate was 12.5% and hospital mortality rate 37.5%.

Results were unimpressive in the four patients having radical surgery, the longest survival being seven months. There were six survivals over one year and three five year survivals. All patients except one died. The living patient was apparently free from malignant disease 11.5 years post-operatively. Cholecystectomy, with its low operative mortality, is the treatment of choice for cholelithiasis and may reduce incidence of malignancy of the gallbladder.

► [The possibility of the practically incurable condition of carcinoma of the gallbladder developing should serve as one of the indications for cholecystectomy when a patient in good general condition is known to have calculi.—Ed.]

**Experimental Induction of Primary Carcinoma of Gallbladder.** Joseph G. Fortner<sup>1</sup> (Memorial Center for Cancer, New York) found primary carcinoma of the gallbladder with invasion of adjacent organs and with metastases in five of six cats that survived 23-32 months after implantation of a single pellet of methylcholanthrene in the lumen of the gallbladder. Eight cats that died 3-10 months after a similar procedure showed no evidence of cancer. Five of six dogs subjected to the same procedure and for a similar period remained alive and well. One dog died after about 30 months' exposure to the carcinogen, but no evidence of cancer was found.

These findings show that the gallbladder epithelium of phylogenetically high animals is susceptible to cancer induction by a compound that is chemically related to naturally occurring substances in bile. The experimental method seems applicable to the study of possible factors concerned with the etiology, pathogenesis and therapy of primary carcinoma of the gallbladder in human beings.

**Congenital Atresia of Bile Ducts. Report of Case Treated Successfully by Cholecystojejunostomy** is pre-

(1) Cancer 8:689-'00 July-Aug. 1955

sented by Rodney Mangot<sup>2</sup> (Royal Free Hosp, London), who notes that the literature reports 38 cases of this condition treated successfully by surgery. Surgery can be performed if atresia exists in the lower hepatic or common duct, or if the gallbladder and cystic duct communicate with the hepatic duct, which is distended with bile. Diagnosis should be made within four or five weeks after birth, because most patients will die of liver failure within five months if blockage is not relieved. Exploratory laparotomy should not be delayed beyond the second month. About 20-25% of the babies with bile duct atresia present conditions correctable only by operation.

Preoperative measures include correction of dehydration, one or two small transfusions and administration of vitamin K. Penicillin is given before and after operation. Ether is the anesthetic of choice. The choice of operation depends on the site and extent of the obliterative process and the condition of the gallbladder.

If choledochoduodenostomy is feasible, the bulbous lower end of the common duct is freed and divided, and a small rubber tube or catheter, about 1.5 cm long, inserted upward toward the hepatic duct. An opening is made in the anterosuperior wall of the first part of the duodenum, opposite the end of the duct, and the catheter is led through the hole into the bowel lumen. With the tube in place, a single row of closely applied interrupted mattress sutures of fine silk or Deknatel, mounted on eyeless needles, is inserted to anchor the wall of the duct to the duodenum.

Hepaticoduodenostomy or hepaticojejunostomy is likewise performed with one row of interrupted mattress sutures, but after the latter, an enteroanastomosis between afferent and efferent limbs of the jejunum is carried out to divert gastric and duodenal contents away from the vulnerable biliary tree. When the gallbladder obviously contains bile (demonstrated by aspiration), the organ may be anastomosed to the stomach, duodenum or a loop of proximal jejunum.

A male infant became jaundiced during second week of life. Congenital atresia was diagnosed. Exposure through a right epigastric muscle split incision revealed an enlarged cirrhotic dark green liver. The spleen was large and a small amount of yellowish ascitic fluid was aspirated. The tiny gallbladder was tensely distended, and the



common bile duct ended in a bulbous projection above the duodenum. Bile was aspirated from the fundus of the gallbladder, then saline solution was forcibly injected to distend the minute ducts. The common bile duct ended abruptly about 2-3 mm below the entrance of the cystic duct. The gallbladder fundus was mobilized, a long loop of proximal jejunum was drawn upward, and the apex of the loop anastomosed to the gallbladder, side to side, using two rows of interrupted sutures of finest silk. Portions of jejunum proximal and distal to the stoma were anchored to the capsule of the liver. Side-to-side jejunojejunostomy was then performed well below the previous anastomosis, to divert gastric and intestinal contents from the biliary tree.

Recovery was uninterrupted, and periodic examinations for three years showed that he was healthy and developing normally.

► [Will the anastomotic opening grow with the child?—Ed]

**Favorable Effect of Cholecystectomy on Coexisting Heart or Coronary Disease** is described by A. Fritsch<sup>3</sup> (Vienna). In 282 patients who had cholecystectomy for cholelithiasis during two years, pathologic ECG changes were observed preoperatively in 49 of 235. Of these 49 with ECG changes, 22 were re-examined 1½-2 years after cholecystectomy. Four had typical angina pectoris, which was completely relieved after operation in three, although ECG remained unchanged in one. In two others the ECG was normal. One patient who had had two myocardial infarcts had fewer anginal attacks after operation, but the ECG was unchanged. All four had chronic cholecystitis with mural infiltration, infection of mucous membrane and numerous gallstones.

Seven of nine patients with symptomatic angina were cured; all had had preoperative ECG signs of circulatory disturbance, which had disappeared at time of follow-up. Two of the seven had acute cholecystitis with symptoms for only 8-14 days, whereas heart symptoms had been present 3 and 14 years respectively. In the other five, gallbladder symptoms had preceded cardiac difficulty. Two patients continued to have anginal symptoms after cholecystectomy, in one, the ECG was unchanged and in the other it became normal.

In two of three patients with myocardial damage and signs of beginning decompensation, there was considerable functional improvement after cholecystectomy, though the ECG remained unchanged. One of these patients had no

cardiac relief. In these three patients, the gallbladder was chronically inflamed, with acute exudation and numerous stones.

One patient with heart symptoms of undetermined origin and signs of circulatory disturbance before operation was completely relieved after cholecystectomy, and the ECG was normal. He had had gallstones for six years; heart disease had been present for two years. The gallbladder was chronically inflamed and contained many stones.

Of five patients who displayed a pathologic ECG pre-operatively, without cardiac symptoms, two with acute cholecystitis had a normal ECG after operation, whereas three with chronic cholecystitis showed no change. Except in one instance, all patients with subjective improvement in cardiac symptoms eventually showed normalization of the ECG. In patients who showed no improvement, the ECG continued to show pathologic changes after cholecystectomy, with one exception.

Indication for cholecystectomy in patients with heart disease must be established by complete clinical investigation and collaboration with an internist. In view of the relation between cardiac and cholecyctic disease, in many cases in which ECG changes and severe heart symptoms might be considered a reason for postponing cholecystectomy, this should be done with the purpose of alleviating the heart condition. In general, signs of decompensation contraindicate surgery, which should be resorted to only in case of great necessity. Recent myocardial infarct also is an absolute contraindication.

► [It has been known for many years that patients with myocardial disease are often benefited by cholecystectomy if the gallbladder is definitely and severely diseased—Ed.]

---

## THE PANCREAS

Etiologic Factors in Pancreatitis Syndrome were determined by R. A. Joske<sup>4</sup> in 70 definite cases and 20 highly probable cases. In 68 cases there was clinical or laboratory evidence of some etiologic factor and in 22 the cause was

(4) Brit. M.J. 2:1477-1481, Dec. 17, 1955.

## GENERAL SURGERY

unknown There were two cases of postoperative pancreatitis, one following cholecystojejunostomy for obstructive jaundice due to carcinoma of the head of the pancreas with hepatic metastases and one following exploration of the common bile duct for obstructive jaundice due to stones in the common bile duct There was no evidence that gallstone impaction and biliary reflux were important etiologic agents in pancreatitis Gallstones were absent in 42 patients and present in 26 and had been present in 14 In only 2 of the 26 were stones detected within the common bile duct and in neither were they impacted at the ampulla of Vater In 14 cases pancreatitis persisted after removal of the stones Cholelithiasis may follow pancreatitis, however, since the latter may cause common bile duct obstruction

Pancreatitis was due to mumps in two patients and to viral hepatitis in eight Pancreaticoduodenitis and hydatid disease of the pancreas were present in one patient each Both acute and chronic pancreatitis may result from general disorders of metabolism Hyperlipemia was present in 6 patients, 17 were alcoholics and 11 were pregnant

Hemochromatosis, sprue syndrome and ulcerative colitis were present in one patient each

A primary vascular disease was considered the etiologic factor in 17 patients These 5 men and 12 women, aged 4 to 81, had either hypertension or significant atherosclerosis Atherosclerosis with or without hypertension, emphysema, cholelithiasis, atrophic gastritis and chronic pancreatitis often appear together in one syndrome

The study demonstrates that pancreatitis is not a disease entity but a syndrome due to different pathologic processes many of which are not initially inflammatory, and should be termed "pancreatopathy" rather than "pancreatitis" It is probable that these differing etiologic factors are reflected by differences in the local pathologic changes within the pancreas and in the natural history of the clinical disease produced It is unjustifiable to treat all patients with "pancreatitis" alike or to assess the prognosis without regard to the probable cause of the disease

**Surgical Considerations in Management of Chronic Relapsing Pancreatitis** are presented by Kenneth W. War-

ren<sup>5</sup> (Lahcy Clinic) The disease is diversified, varying in etiology, duration, localization and extent The central pathologic alteration is partial or complete intrapancreatic obstruction Associated disease of the biliary and gastrointestinal tract is common The physiologic consequences may affect both acinar and islet functions Indirect surgical procedures, such as cholecystectomy, choledochostomy, biliary-intestinal anastomosis, sphincterotomy, gastroenterostomy, pyloric exclusion, gastrectomy, sympathectomy and vagotomy, have limited value in treatment

Direct surgical methods, aimed at the pancreas itself, give the best surgical results Cystic collections, which occurred in about 25% of the author's patients, should be drained Multiple pancreatic stones are common, and pancreatolithotomy must be done, usually in combination with other procedures Ligation of the pancreatic ducts should not be done Occasionally, anastomosis of the duct of Wirsung to the upper jejunum is used with other procedures Transduodenal exploration and dilatation of the ducts of Wirsung and Santorini are valuable Distal pancreatectomy is indicated when the pathologic process is confined to this part of the organ, together with anastomosis of the divided duct of Wirsung to the jejunum it may prove effective even when the entire gland is involved Pancreatoduodenectomy is one of the most effective procedures because it eliminates the point of obstruction, which is most frequently in the region of the periampullary portion of the duct The procedure is formidable and should not be embarked on lightly If pancreatoduodenal resection is done, the divided duct of Wirsung should be anastomosed routinely to the jejunum by precise mucosa-to-mucosa approximation to restore the external pancreatic secretions to the intestinal tract Total pancreatectomy has been performed in a few instances, but mortality is high

There is no single surgical maneuver, short of total pancreatectomy, which is but rarely justifiable, that will answer all surgical requirements for treating the disease

Of 87 patients treated surgically, all had abdominal pain, 56% used alcohol excessively, 48% used narcotics excessively, 94% had weight loss, 38% had diabetes, usually

mild, 41% had pancreatolithiasis, 25% had pancreatic cysts and 25% had jaundice. There was no hospital mortality, and only 2 of 58 patients with direct operation on the pancreas had serious complications. Both had prolonged pancreatobiliary fistulas. The 58 direct surgical procedures included 13 pancreatoduodenal resections, 1 total pancreatectomy, 10 distal pancreatectomies, 5 pancreatogastrostomies, 2 pancreatojejunostomies, 20 transduodenal explorations of the pancreatic ducts, 5 drainages of pancreatic cysts and 2 pancreatic abscesses. The other patients had indirect surgical procedures.

Cholecystectomy and choledochostomy had little effect on the disease. Of nine patients with thoracolumbar sympathectomy, three had good results and two fair. Gastroenterostomy in one patient was unsuccessful. Of 10 with sphincterotomy, 5 had good results. All five with pancreatogastrostomy had good results. Two had pancreatojejunostomy, in one, a pancreatic abscess developed, and the other showed good results. Distal pancreatectomy produced good results in 9 of 10. Of 13 with pancreatoduodenal resection, 3 died subsequently, and 8 had good results. One patient with total pancreatectomy had good results. Of 20 with transduodenal dilatation of the main pancreatic ducts, 16 had good or excellent results. High incidence of alcohol and narcotic addiction makes follow-up of patients difficult.

**Eight Year Study of Pancreatitis and Sphincterotomy** is presented by Henry Doubilet and John H. Mulholland<sup>6</sup> (New York Univ.). Recurrent pancreatitis is primarily due to a physiologic dysfunction of the sphincter of Oddi, which in the presence of a common passageway, allows bile to enter the pancreatic duct under tension. This passageway was demonstrated at operation in 316 patients, either by direct observation during transduodenal sphincterotomy or by cholangiography. Diagnosis of acute pancreatitis is based on a high serum amylase level although a low level does not rule out the disease. In chronic pancreatitis there is a low response to secretin, although normal response to the secretin test does not exclude the disease. A history of previous attacks of pain and x-ray evi-

dence of calcification of the pancreas are good evidence of chronic pancreatitis

Treatment of acute pancreatitis is nonoperative and consists of continuous nasogastric suction for three days or until serum amylase levels are normal, administration of anticholinergic drugs (atropine or pro-banthine®) to reduce secretion and relax the sphincter, sedation with demerol® and phenobarbital to relieve pain and anxiety, and administration of fluids and electrolytes to replace losses and of antibiotics to combat secondary bacterial invasion or exudates and necrotic tissues. The patient is given fat-free liquids, a fat-free soft diet, and full fat-free diet on successive days after removal of the nasogastric tube.

After recovery from the acute attack is complete, sphincterotomy is performed. Sphincterotomy abolishes pain due to distention of the biliary-pancreatic-duct system, prevents further attacks of acute inflammation due to reflux, stops progressive destruction of the pancreas and allows it to regenerate. By diminishing the intraductal pressure in the pancreas, sphincterotomy results in the cure of pseudocysts, cysts and pancreatic fistulas. The operation will fail if the patient is not kept on a fat free and alcohol free diet until regeneration is maximal. Sphincterotomy must be accompanied by cholecystectomy, whether the gallbladder is normal or not.

**TECHNIC**—An operative cholangiogram is made first then the gallbladder removed. The sphincter of Oddi is sectioned either endocholedochally by a special instrument or by the following technic transduodenally. A plastic balloon tube is passed through the cystic or the open common duct into the incised duodenum and pulled down until the balloon lies in the ampulla. The balloon is then inflated and the papilla pulled through the incision and held by three traction sutures. The plastic tube is withdrawn and a punch is used to cut the sphincter for a distance no greater than 8-10 mm. A plastic tube can then be placed in the pancreatic duct for pancreatographic studies. No reparative sutures are placed on the sectioned sphincter because of the danger of obstructing the terminal part of the pancreatic duct.

Follow-up of at least two years on 190 patients revealed good results (absence of symptoms and gain in weight) in 169 and poor results (persistence of gastrointestinal symptoms but no pancreatitis) in 4. There were 17 failures. Nine patients died postoperatively, one patient died of carcinoma of the pancreas. Five patients with severe chronic

alcoholism and two psychoneurotics continued to have symptoms

**Operative Contrast Visualization of Pancreatic Disease** is helpful in elucidating the pathologic process and of practical assistance in technical manipulations. The method used by Henry Doubilet and John H. Mulholland<sup>7</sup> (New York Univ.) consists of initial cholangiography by special technic and subsequent pancreatography.

**TECHNICS**—*Cholangiography*—Diodrast,\* urokon\* or neo iopex\* (35-50%) is injected slowly through a long rubber tube, to which is attached a short beveled needle (no. 18). The needle is inserted into the cystic duct or into the common duct if the cystic duct and gallbladder have been removed. Simultaneously, 30 cc of N/HCl is instilled into the duodenum through a Rehfuess tube inserted through the mouth before operation. The acid creates a spasm in the sphincter of Oddi. If a common passageway is present, the radiopaque solution ascends into the pancreatic duct. Two exposures usually are made duodenally, a fine plastic tube is inserted 4-5 cm into the duct of

*Pancreatography*—After section of the sphincter of Oddi trans-Wirsung in the posterior wall of the ampulla of Vater. Radiopaque solution (70%) is injected slowly, about 10 cc in five minutes, the last 2 cc is introduced during x-ray exposure. The excess flows into the duodenum around the tube or through the accessory duct of Santorini, if present. If the pancreatic duct is dilated or the pancreas has been incised, the plastic tube is left in place for drainage. Two sutures are placed to hold it to the sectioned sphincter, and the tube is led up the common duct and out through the cystic duct or alongside a T tube in the common duct (Fig. 94). Regression of inflammation or of cysts can be followed by postoperative serial pancreatographic studies.

With cholangiography, stones in the common duct, especially at the ampulla of Vater, can be detected. These may cause spasm of Oddi's sphincter and may allow reflux of bile up the pancreatic duct. The diameter, direction and curvature of the common duct and direction of its insertion into the duodenum, degree of narrowing of a common passage-way of the common duct and presence of edema is present, the whole can also be determined. When edema is present, the whole pancreatic duct is delineated, and sometimes, with severe inflammation, smaller pancreatic ducts can also be seen.

In the absence of acute inflammation, pancreatography delineates only the main pancreatic duct system. Presence of a communicating duct of Santorini can be demonstrated

if radiopaque injection is continued during x-ray exposure. Dilatation of the pancreatic duct due to persistent spasm of Oddi's sphincter, and partial or complete organic obstruction, due to stone, previous operation or carcinoma, can be demonstrated.

In case of complete obstruction, the acinar tissue behind the obstruction atrophies. Removal of the obstructed portion is not necessary and may even produce harm from

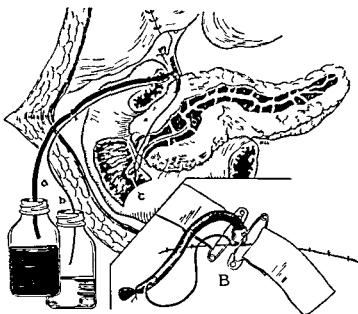


Fig 94—Polyvinyl tube (b) passes alongside T tube (a), through lower end of T lying in common duct, through cut sphincter of Oddi (c), and up pancreatic duct. Bile and pancreatic juice are collected separately. After four days T tube is tied and polyvinyl tube inserted into it by means of needle (inset B), allowing pancreatic juice to circulate back into duodenum. In absence of T tube, plastic tube is brought out through cystic duct. (Courtesy of Doubilet, H., and Mulholland, J. H.: *S. Clin. North America* 36:385-403, April, 1956.)

loss of islet tissue. In partial obstruction caused by a stone, removal of the stone by direct incision and drainage by an inlying plastic tube may allow the pancreas to regenerate. Partial obstruction by stricture should be treated, if technically feasible, by implantation of the distal dilated duct into the jejunum. If the stricture is close to the tail, excision of the tail to the point of stricture may be necessary. If a radical procedure is not feasible in partial obstruction caused by cancer, back pain can be prevented by drainage of the obstructed duct through a plastic tube.

If as a result of necrosis one or more small pancreatic ducts rupture, pancreatic juice will accumulate retro-



toneally if intraductal tension is high. Exudate and pancreatic juice may dissect downward to the sigmoid or anteriorly between the leaves of the mesocolon, to cause obstruction of the transverse colon or form a pseudocyst between stomach and colon. It may spread upward to form a subphrenic collection or along the aorta into the posterior mediastinum. For pseudocysts on the right side beneath the head of the pancreas adequate drainage must be achieved through Wirsung's duct and the pseudocyst must also be drained. Prognosis must be guarded. Pancreatic fistulas formed by marsupialization of a pseudocyst or accidentally incurred during gastric resection, should be treated on the same principle of reducing pancreatic intraductal pressure by sphincterotomy. At operation, pancreatography will reveal clearly the connection between duct and fistula. True acute cysts of the head of the pancreas can be eliminated by drainage of the pancreatic duct through the duct of Wirsung. Chronic true cysts of the head are usually thick walled and noncollapsible and have lost continuity with the main pancreatic duct. They can be visualized by injecting radiopaque solution after aspirating their contents. Excision is difficult but cystojejunostomy is satisfactory treatment.

Loss of semipermeability of the duct epithelium as a result of inflammation permits seepage of pancreatic juice into pancreatic tissues hence radiopaque material opacifies the acutely inflamed portion of pancreas. As inflammation subsides, opacification disappears. If a 70% radiopaque solution is injected to visualize the pancreatic duct system and another injection given after 10 minutes (to allow for inflammatory reaction to concentrated radiopaque solutions), the whole pancreas will be opacified and an adenoma or other tumor not connected with the ducts would be revealed as a nonopacified space.

Pancreatography is no more difficult than operative cholangiography and is without danger. It has proved valuable in demonstrating normal and abnormal anatomy of pancreatic ducts and tissues in demonstrating etiologic and pathologic features in progressive recurrent pancreatitis and in establishing therapy on a physiologic basis.

**Direct Pancreatography during Operation in Pancreatic Retention.** C. Nardi and J. Lataste<sup>8</sup> (Paris) point out that,

(8) *Presse med.* 63:957-958, June 1955.

despite numerous published reports, retrograde pancreatography has never enjoyed great favor because of difficulties that may be encountered in locating the papilla of Vater and in catheterizing the pancreatic duct. In performance of this procedure on over 50 patients, failures were exceptional and complications were met with in only one patient over 60, with hypertension and atheromatosis, who had had hemiplegia some months previously. Hence the procedure is not advised in hypertensive patients who have had vascular accidents and painful epigastric crises suggesting subacute recurrent pancreatitis.

Difficulties accompanying retrograde pancreatography suggest that direct pancreatography may become important in certain cases in which suitable therapy is dependent on roentgenologic findings. The authors often use this technic in pathologic anatomic studies, because of its relative simplicity, and report a case in which it was applied clinically.

Man, 56, had recurrent pain and icterus with severe hyperglycemia seven months after choledochoduodenal anastomosis for relief of symptoms caused by cancer of the head of the pancreas. On re-exploration, attempted retrograde catheterization of the pancreatic duct after duodenotomy was unsuccessful; the catheter penetrated only 1-2 mm. into the ampulla of Vater. Since extent of the pancreatic lesion could not be determined macroscopically, direct pancreatography was performed after removal of the spleen. The tail of the pancreas was sectioned 3 cm. from its tip, and the pancreatic duct was catheterized (with some difficulty, because of its tortuosity) and 4 cc. of 50% diodone was injected. Pancreatography confirmed the diagnosis of massive tumor of the head of the pancreas which compressed the pancreatic duct and caused enormous dilatation. Caudal pancreaticojejunostomy gave satisfactory relief.

The authors suggest that if laparotomy discloses a significant mass in the head of the pancreas, operative cholangiography should first be done, especially if the patient is jaundiced. If this shows patency in the lower portion of the bile duct, then retrograde pancreatography should be attempted after duodenotomy, because it is likely that the pancreatic duct can be catheterized. But if the bile duct is partially or completely stenosed, it is more than likely that the pancreatic lesion also compresses the pancreatic duct. In such cases, splenectomy should not be avoided. Risk is minimal and is justified when all therapeutic indications depend on results of pancreatography.

## Resection for Carcinoma of Head of Pancreas. Two Five Year Survivals are reported by E G Muir<sup>9</sup> (London)

CASE 1—Man, 60, had a long history of indigestion. Diagnosis of chronic duodenal ulcer with duodenal deformity was made. Laparotomy revealed a localized and movable mass in the head of the pancreas. Metastases were not found. The head of the pancreas, pyloric antrum and duodenum were resected and the oversewn neck of the pancreas implanted into the first loop of jejunum between the common bile duct and the divided end of the stomach. Recovery was uneventful. Histologic diagnosis was colloid or mucinous adenocarcinoma of the pancreas. He did well for two years, except for failure of fat absorption with loose pale stools. A small carcinoma of the transverse colon was resected three years later. No evidence of metastases was found and the anastomoses of the first operation seemed good. He continued well for five years after the original operation except for difficulty with fat digestion. A small laparotomy incision was made in the fifth postoperative year to determine the cause of suggested compression of the stomach seen on barium swallow. No metastases were found and the distortion was due to the position of the stomach.

CASE 2—Man, 58, had jaundice for four weeks. Laparotomy revealed a small growth at the ampulla of Vater. Metastases were not found and resection of the head of the pancreas and the duodenal loop was performed. The oversewn neck of the pancreas was implanted into the first jejunal loop between the common bile duct and the divided end of the stomach. Recovery was uneventful. Histologic diagnosis was papillary adenocarcinoma of the ampulla of Vater. He had no weight loss or diarrhea and little evidence of fat wastage in the stools. The gallbladder was removed nine months postoperatively for stones. He made an excellent recovery. He was still alive and well seven years after the first operation and free from recurrence.

► [Wonder why the author designates the second case as a carcinoma of the head of the pancreas? His description places it as having arisen in the ampulla of Vater. It is well known that the prognosis of ampullary carcinomas is better than that of cancers arising in the pancreas. See the following abstract for more examples of five year survivors.—Ed.]

**Survival for More than Five Years after Pancreatoduodenectomy for Cancers of the Ampulla and Pancreatic Head**  
Clarence Dennis (State Univ of New York, New York City) and Richard L Varco<sup>1</sup> (Univ of Minnesota) present three patients with cancer of the ampulla of Vater who have survived more than 12, 10 and 9 years, respectively, after resection and two with cancer of the head of the pancreas who have survived more than 9 and 6 years. The cancer has apparently been truly eradicated in one of the latter.

The prognosis of pancreatic and ampullary carcinomas is

(9) Brit J Surg 42 489 490 March 1955

(1) Surgery 39 92 106 January 1956

not appreciably worse than the outlook in cancer of the stomach. Accurate status of the tumor is established at exploration by adequate exposure, freeing of the right border of the duodenum to permit inspection and palpation from behind, inspection of the hepatic artery and mesenteric vessels and search for metastases to nodes and liver. Biopsy at the time of exploration is not helpful and has proved dangerous because of continued pancreatic leakage in patients not subjected to resection. The surgeon must bear the responsibility for the decision whether or not to resect.

Radical resection in a one stage procedure should be done if there is a localized mass without distant evidence of spread. The operation consists of removal of one fourth to one half of the stomach, all of the duodenum, a few centimeters of the jejunum, head and neck of the pancreas, all of the common bile duct, a short segment of the common hepatic duct and the gallbladder and cystic duct. In two of the reported cases 12 hours were required for the operative procedure. Meticulous sharp dissection, careful hemostasis and the fine silk technic are important for good results. The frequency of anomalies in the area emphasizes the need for care. In two cases the hepatic artery arose in anomalous fashion, traversing the head of the pancreas in one.

Biliary anastomosis, when possible, should be made high in the common hepatic duct, with resection of the duct system below, because the cancer may have extended up the common bile duct. The gastric anastomosis should be 40 cm caudal on the jejunum to the end to end biliary anastomosis to avoid regurgitation of intestinal contents, provide a wide stoma and prevent ulceration at the gastrojejunal anastomosis. The pancreatic anastomosis has not been followed by pancreatic fistulization. Total resection of the pancreas has been suggested by some surgeons because cancer cells have been found floating in the fluid in the dilated pancreatic duct. It remains to be seen whether the advantages of avoiding occasional seeding through cells suspended in the fluid outweigh the known complications of total pancreatectomy.

**Aberrant Pancreatic Carcinoma in Jejunal Diverticulum.** Frederick G. Zak<sup>2</sup> (Manhasset, Long Island, N. Y.) describes one case.

Man 30 had back pain and intermittent fever for a month. A large upper left abdominal mass was palpable. The mass was shown on x ray to displace intestinal loops and contain a fluid level and it opened into the jejunum. Surgery revealed a firm grayish bosselated centrally cystic mass behind the stomach and intimately adherent to loops of small intestine, pancreas and retroperitoneal structures. Frozen section disclosed anaplastic carcinoma and the abdomen was closed. The patient died six days later.

Autopsy revealed the tumor to be attached to the colon and pancreas by loose connective tissue. A narrow fistulous opening surrounded by a whitish elevated rim communicated between the upper jejunum and the cavity within the tumor. The large irregular cavity was filled with murky fluid. Microscopic study showed an epithelial growth of organoid appearance resembling pancreas and composed of grouped cells with abundant amphophilic cytoplasm. A section from the rim of the jejunum opening disclosed a spindle cell tumor with intercellular reticulum formation and gradation to the epithelial growth. The diagnosis was aberrant pancreatic carcinoma.

**Functioning Metastases from Islet Cell Tumor of Pancreas.** Control with Corticotropin (ACTH) is reported by Conrad J. Baumgartner and John L. Reynolds<sup>3</sup> (St. Vincent's Hosp., Los Angeles).

Woman 59 had dizzy spells in 1944. Fasting blood sugar content was 85 mg/100 ml. In 1952 she had a hysterectomy for fibroids and exploration revealed a hard irregular sized tumor in the tail of the pancreas. Fasting blood sugar level on the fifth postoperative day was 108 mg. She had nausea and dizzy spells. At reoperation the tail of the pancreas, omentum and spleen were removed. The diagnosis was islet cell carcinoma with tumor emboli within the pancreas and metastases to the lymph nodes. One year later she had vertigo, nausea, diplopia, a tremor and numbness of the mouth and tongue. The liver was enlarged and irregular and blood sugar content was 33 mg. The symptoms were relieved with intravenous administration of glucose. A glucose tolerance test revealed an initial rise in the blood sugar level which returned to normal in six hours.

A third operation revealed liver metastases and biopsy showed islet cell carcinoma. She continued to have symptoms of hypoglycemia which were relieved by administration of 40 units of corticotropin gel daily and then every third day. Fasting blood sugar level was now 79 mg. While she was taking corticotropin the blood sugar during a glucose tolerance test did not reach low levels. During the next year the level remained fairly normal on corticotropin. X ray of the chest was negative and the liver edge was no longer palpable. The glucose tolerance test showed marked utilization of the glucose and no hypoglycemia.

This is believed to be the first reported case in which hypoglycemia from a functioning metastatic islet cell tumor has been controlled for one year with corticotropin gel.

► [One is reminded that the first case of recognized islet tumor was a carcinoma with functioning metastases in the liver. It was diagnosed by Russell Wilder of the Mayo Clinic in 1927 and an exploratory operation was performed by Will Mayo. Assays of some of the metastatic tissue in the liver showed a high content of insulin.—Ed.]

**Marked Hypoglycemia Associated with Nonpancreatic Tumors.** Richard S. Silvis and Daniel S. Simon<sup>4</sup> (U.S. Naval Hosp., Oakland, Calif.) present one case.

Man, 23, had weakness, confusion, was withdrawn and fainted a few times in the mornings. He was found in a coma one morning and a mass was discovered in the right upper quadrant. Blood sugar was 35 mg./100 ml. In the right flank was a large, hard mass that was palpable anteriorly and posteriorly. In the right upper quadrant, separate from the large mass, was a firm, ovoid lobular mass, 10×6 cm. in size. X-rays revealed the large mass in the right upper quadrant with small calcifications. He became comatose for a second time and the blood sugar was 32 mg./100 ml. He responded to intravenous glucose administration. Retrograde pyelography and retroperitoneal air insufflation showed a large mass in the flank that was extrarenal. The small firm mass in the right upper quadrant was the right kidney. Control of hypoglycemia was accomplished with about 400 Gm. glucose daily. Through a right lumbar incision a large encapsulated tumor of the iliopsoas muscle was removed. The tumor extended between the transverse processes of the 1st to 3d lumbar vertebrae. The operation was difficult, and required 6,000 cc. blood. He did well postoperatively and glucose requirements returned to normal. Lumbar myelogram revealed residual tumor in the spinal column and this was removed.

The tumor weighed 1,200 Gm. and microscopically was a fibroma. The patient was asymptomatic after surgery and had no hypoglycemic episodes.

The cause of the hypoglycemia associated with large retroperitoneal tumor is unknown.

**Surgery of Annular Pancreas: Summary of 60 Patients Operated Upon** is presented in a collective review by Morton J. Tendler and Andrea Ciuti<sup>5</sup> (Univ. of Tennessee), with two personally observed cases. Signs and symptoms of annular pancreas depend on degree of duodenal obstruction. Complete obstruction, showing the classic "double bubble" x-ray finding, requires surgery shortly after birth. Incomplete obstruction is accompanied by transient symptoms, with weeks or months between attacks; x-ray diagnosis is most accurate during remissions. Minimal obstruction is an incidental finding at operation or autopsy. Coexistence of gastroduodenal ulcers can make diagnosis difficult, especially when duodenal scarring complicates the x-ray pic

(4) New England J. Med. 254:14-17, Jan. 5, 1956.

(5) Surgery 38:298-310, August, 1955

ture Various authors have used different procedures with success When annular pancreas presents a simple bandlike constriction, duodenojejunostomy seems to be preferred When massive enlargement of the annulus precludes this, gastroenterostomy is successful These procedures are indicated most often in newborns and infants When pancreatic disease and duodenal obstruction are found, subtotal gastric resection with gastrojejunostomy has been performed with success When jaundice is present, cholecystenterostomy has been suggested The gallbladder should not be removed

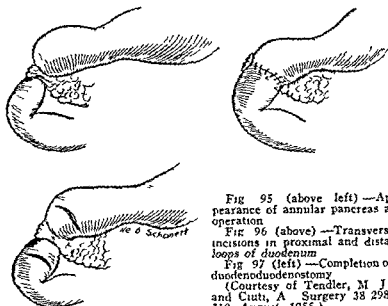


Fig 95 (above left) — Appearance of annular pancreas at operation

Fig 96 (above) — Transverse incisions in proximal and distal loops of duodenum

Fig 97 (left) — Completion of duodenoduodenostomy  
(Courtesy of Tendler, M. J. and Ciuti, A. *Surgery* 38:298, 310 August 1955)

unless seriously diseased Pancreatic resections are always dangerous, but in most reported cases results have been good Sectioning of the annulus should be avoided, however, when possible

**CASE 1**—Man 46 had had almost annual attacks of severe digestive disorder incapacitating him for a week or two X-rays showed only a bubble of barium in the proximal duodenum, which did not disappear until after duodenal suction At operation, a ring of pancreatic tissue practically surrounded the duodenum (Fig 95), narrowing the lumen to about 1.52 cm Duodenum proximal to obstruction was 7-8 cm in diameter edematous and thickened The distal limb was normal (3.5-4 cm) and freely movable Duodenoduodenostomy anterior to the obstructing ring was successful (Figs 96 and 97)

**CASE 2**—Boy, aged 1 had had severe vomiting spells, with constipation, almost weekly since birth X-ray showed 40% retention in stomach after three hours Duodenal cap and proximal loop were

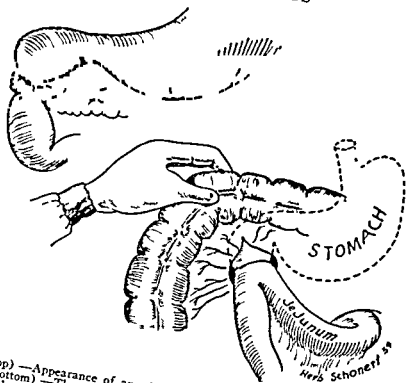


Fig 98 (top) — Appearance of annular pancreas at operation.  
 Fig 99 (bottom) — The ideal operation of choice transmesocolic duodenojejunostomy is completed  
 (Courtesy of Tendler M J and Ciuti V Surgery 38 298 310 August 1955)

distended and filled with barium. An obstructing pancreatic capsular band about 1 cm wide was found at operation (Fig 98). Retrocolic duodenojejunostomy (Fig 99) was followed by disappearance of symptoms and satisfactory weight gain.



## THE ESOPHAGUS

**Esophageal Atresia** Importance of Early Diagnosis and Adequate Treatment Illustrated by a Series of Patients

Esophageal atresia is not uncommon, and prompt diagnosis and corrective surgery can save many infants. The four main types are (1) atresia with no tracheoesophageal fistula and usually with widely separated segments, (2) atresia of the distal segment with a proximal segment entering the posterior wall of the trachea, (3) atresia with the lower segment of esophagus entering the posterior wall of the trachea at or above the carina and (4) loss of continuity of the esophagus with both the proximal and distal segments entering the posterior wall of the trachea.



H William Clatworthy<sup>6</sup> (Ohio State Univ) reviewed 35 cases occurring between 1946 and 1954. In 29 infants, a one stage operation, consisting of division of the tracheoesophageal fistula and end-to-end anastomosis of the esophagus, was possible. Of the 35 infants, 33 had type 3 anomaly. Only two infants had absence of a large segment of esophagus, making primary anastomosis impossible and necessitating accomplishment by stages or by more complicated procedures. There were eight associated anomalies, five of which proved fatal.

Eight infants were premature, and polyhydramnion was found in three instances. Excess mucus choking and intermittent cyanosis are early symptoms. Frequent suction is required. Acute gaseous abdominal distention was noted in two infants. This condition is primarily due to a large tracheoesophageal fistula, permitting the pumping of air into the stomach. Later symptoms include inability to retain feedings, immediate regurgitation and cyanosis with attempted feeding and progressive development of aspiration pneumonitis. Diagnosis can be established by inability to pass a no. 8 or 10 catheter into the stomach. Failure to pass the catheter beyond 10-15 cm from the tip of the nose is diagnostic. Types 2 or 4 lesions can be further demonstrated by injection of 0.5 ml (or less) lipiodol<sup>®</sup> into the esophagus. The oil should be removed immediately. Barium should never be used.

Treatment should be carried out by persons well qualified to take care of surgical pediatric problems. Preoperatively, the infant is well hydrated, placed on constant esophageal suction and put into an incubator. A plastic tube is placed in the greater saphenous vein for administration of fluids. The best anesthesia is endotracheal cyclopropane with oxygen.

Of the 29 infants in whom a definite corrective procedure was performed, 12 died, including 5 in whom a transpleural approach to the esophagus was used. Only two of the eight premature infants survived. Atelectasis and pneumonia caused death in seven; pulmonary edema in two and cardiac anomaly in one. Only 4 of 17 survivors had strictures of the esophagus requiring dilatation. Most successfully treated infants have a brassy cough for six months to two years.

(6) *Pediatrics* 16:122-128, July 1955.

and are more susceptible to upper respiratory infections. Most infants can take a simple solid diet by age 2.

**TRACHEA—**Anastomosis is best performed by an extrapleural approach through the bed of the third, fourth and fifth ribs on the right side through a parascapular hockey stick incision.

After division of the azygos vein and identification of the vagus nerve, the tracheoesophageal fistula is freed up and transected close to the trachea. The tracheal opening is carefully closed with two layers of running 5/0 black silk Deksnel suture. The proximal pouch is then identified by having the anesthesiologist push it down into the operative field with the intubating catheter. A traction suture is placed through the apex of the pouch and it is further freed from the trachea to which it is intimately attached. The end-to-end anastomosis between the large proximal pouch and the small distal fistula is then accomplished using two layers of interrupted 5/0 Deksnel suture. Traction sutures are placed between the proximal pouch and the prevertebral fascia or vagus nerve to provide fixation and promote sealing of the anastomosis. The chest is then closed in layers with interrupted 5/0 silk.

Gastrectomy is performed immediately after the initial surgery or one or two days later.

Postoperative care includes incubation, suction of the esophagus, antibiotics, gastrostomy feedings until the infant can swallow, which is usually about 10 days postoperatively, and oral feedings as soon as they can be taken.

Gastroesophageal "Sphincter" and Mechanism of Regurgitation are discussed by Paul Marchand<sup>7</sup> (Guy's Hosp., London). Physiologic delay to passage of food from the esophagus into the stomach occurs on deep inspiration and during the Valsalva test and is due to differences in pressure between the thoracic and abdominal cavities. The delay is only temporary, as the esophageal peristaltic wave can overcome the pressure differential. Pathologic delay to the passage of food in achalasia of the cardia and mild cases of acute caustic injury are due to failure of the terminal esophagus to relax. Regurgitation from stomach into esophagus is prevented by the oblique entrance of the esophagus into the stomach and the resting muscle tone of the terminal esophagus, which maintains a closed lumen at the junction of esophagus and stomach. The tonic closure of the esophagogastric junction is inhibited by swallowing and by the arrival of a peristaltic wave at the lower esophagus. If the intragastric pressure is high, the resisting mechanism may be weakened at the moment of swallowing, permitting re-

gurgitation The diaphragm cannot constrict the terminal esophagus and plays no part in preventing regurgitation

Regurgitation can occur by an increase of the intragastric pressure above levels normally withstood by the resisting mechanism This type of regurgitation can be passive or active Alteration of the normal esophagogastric angle as in sliding hiatus hernia and inhibition of the tone of the terminal esophagus, as during swallowing, can cause regurgitation

Symptoms of passive regurgitation include flatulence or passage of gastric air in the erect position, fluid regurgitation when bending forward or lying down, and pain The pain is usually choking or boring and is felt in the front of the chest or neck or vaguely in the midline occasionally it radiates A sensation of burning may arise from the esophagus

Causes of regurgitation include occasional reflux dyspepsia from dietary indiscretions, adiposity, cholecystitis and duodenal ulcer, air-swallowing, pregnancy and hiatus hernia One or more of the following factors is always present in any case of clinical regurgitation change in posture, gastric distention, diminished peritoneal capacity, as in pregnancy adiposity and large abdominal tumors, swallowing, and loss of the normal gastroesophageal angle as occurs in hiatus hernia The symptoms of these various pathologic conditions are all the same because the effect of each is to cause regurgitation Reflux of stomach contents into the esophagus may be asymptomatic, especially after meals Even though the intensity of symptoms varies so widely, these are in no way specific for they are due to regurgitation and not to the underlying cause The more persistent the regurgitation, the more severe the symptoms, which are caused by prolonged irritation of the esophageal mucosa

**Spontaneous Rupture of Esophagus, with Presentation of Four New Cases** George W B Starkey<sup>8</sup> (Boston) stresses that the mortality rate following spontaneous rupture of the esophagus is still too high because diagnosis is not made soon enough and proper treatment is instituted too late These ruptures are not truly "spontaneous" for they do not occur without extrapleural provocation, principally vomit-

ing Most common mistaken diagnoses are perforated peptic ulcer, acute myocardial infarct, spontaneous pneumothorax, acute pancreatitis, dissecting aortic aneurysm and acute mesenteric thrombosis

Onset is usually acute Chest pain, particularly in the back, is aggravated by breathing Unremitting pain often radiates to the upper abdomen and shoulders The patient usually becomes tachypneic and is in shock, often groaning in agony despite heavy medication Often the upper abdomen is spastic, with fluid or air and fluid in the left, or sometimes the right chest As swallowed air escapes from the rent in the esophagus, it begins to dissect up through the mediastinum into the subcutaneous areas of neck and face If the perforation extends into the pleural space, it may cause tension pneumothorax Chest x rays often show fluid levels in the mediastinum and a hydropneumothorax A swallow of lipiodol<sup>2</sup> almost invariably demonstrates the esophageal leak

Preoperatively, oxygen and moderate doses of an analgesic should be given, and hemoconcentration or other fluid and electrolyte imbalance corrected, along with large doses of antibiotics If the patient is in shock and has a hydropneumothorax, particularly if under tension, closed thoracotomy drainage may convert a precarious situation to a tenable one Thoracotomy is performed and the esophageal tear closed with two layers of interrupted fine silk sutures Pleural and mediastinal spaces are drained If the diagnosis is made 36-48 or more hours after esophageal rupture, only closed thoracotomy drainage is needed, followed by a feeding jejunostomy a day or two later

Pathologic examination shows dark brown fluid and fibrin in the pleural space and, if the mediastinal pleura has ruptured, also gastric contents The mediastinal pleura often is fiery red with some areas of gray or brown slough The esophagus has a vertical tear 2-5 cm long in its lateral wall just above the diaphragm There appears to be no underlying disease to account for the rupture

Three of four patients described had esophageal rupture associated with severe vomiting, in the fourth it was associated with yawning and stretching A sudden increase in intra abdominal and therefore intragastric pressure was a basic factor in three cases Initial diagnosis was incorrect

in all, resulting in delays of 12 hours to 8 days until operation. Three patients were treated by primary closure of the esophageal tear, with two survivals. One, aged 75, died the fifth postoperative day of a second myocardial infarct. One, 69, in whom pleural drainage was instituted eight days after rupture, died three weeks later of massive hemorrhage and perforation of a duodenal ulcer.

► [It is well to call attention to this serious condition because it is seldom diagnosed promptly. Yet the diagnosis usually is not difficult if one thinks of the possibility.—Ed.]

**Spontaneous Rupture of Esophagus** is little known, and most texts fail to mention it as one of the acute emergencies. Because clinicians, confronted with a probable case, as a rule do not think of this diagnostic possibility, M. Rios Mozo<sup>9</sup> (Univ. of Seville) reviews the record of a patient he observed, as a student, with Mozo Rodriguez, who reported it in 1946 as a *questionable instance of perforation by a gastric ulcer into the pleural cavity*. At that time it was the subject of a lengthy conference by eminent clinicians, but none recognized that the severe fatal illness probably had been due to spontaneous rupture of the esophagus. Unfortunately, autopsy had not been permitted. Later it became evident that this patient had presented the classic clinical picture of esophageal rupture.

The patient with a ruptured esophagus has a history of repeated or continuous vomiting preceding sudden onset of severe pain, localized in the upper abdomen, in the epigastrium or lower thorax, it may be retrosternal and often is diffuse and difficult to localize. Other classic signs are subcutaneous emphysema of the neck, dyspnea due principally to invasion of the pleural cavity (especially the left) by gastric contents and intense shock. The accident may be complicated later by mediastinitis and empyema.

Turbulence of intraesophageal pressure caused by violent nausea and vomiting, with general or local changes in the esophageal wall, are etiopathogenic factors. Rupture usually occurs in the left posterolateral wall of the lower third of the esophagus.

Prognosis is extremely grave unless the condition is recognized immediately. Then, after treatment to counteract shock, suture of the esophageal tear should be attempted;

this has been successful in saving life in several instances. Importance of this contingency should be kept in mind whenever an acute abdominal or thoracic emergency is encountered. Differentiation must be made from gastroduodenal ulcer, angina, acute coronary thrombosis and acute pancreatitis.

**Benign Muscle Wall Tumors of Esophagus: Report of Two Cases** These tumors are rare, compared to carcinoma, and neoplastic change is more likely to involve the mucosa than the muscle layer. In a 30 year series from the Mayo Clinic, there were 18 cases of leiomyoma or leiomyosarcoma and 2,312 cases of carcinoma. Besides polypoid tumors, the most common benign tumors are those arising in muscular layers, characterized by slow growth, usually relatively small size and mediastinal extension. Symptoms may be absent or appear comparatively late. These muscle wall tumors are often incidental findings at autopsy.

Establishment of the correct diagnosis of benign esophageal tumors is not always easy, as illustrated in the cases reported by O Perasalo and E Laustela<sup>1</sup> (Helsinki). Chief symptom in a case of leiomyoma in a man, 35, was dysphagia for 10 years that progressed in severity. Although the tumor was relatively large and encircled the esophagus intramurally, the patient could ingest all types of food. In a man, 52, with a pedicled fibromyoma in the lower esophagus, dominant symptoms were pain in the substernal and upper abdominal regions and typical digestive symptoms. There was no hemorrhage in either case.

The leiomyoma was adherent to the muscular layer, encircled the esophagus spirally, was 28 cm long and weighed 92 Gm. Entire length of the esophagus was dilated, as often seen with myoma. The fibromyoma in the second case was relatively small ( $2.5 \times 1.5$  cm) and submucous and had a stalk 4 cm long giving it a range of movement of 8 cm. For this reason it was not visualized on esophagoscopy, because it slid downward into the stomach.

Preoperative diagnosis could be made with considerable certainty in the first case on the basis of pneumomediastinography. The usual thoracic x-ray and contrast medium examination of the esophagus pointed toward a mediastinal

(1) *Ann. chir. et gynaec. Fenniae* 44:145-156, 1955.

tumor In the second case, examination with contrast medium indicated a tumor close to the cardia, but the definitely outlined defect was not typical of carcinoma

Both patients were completely asymptomatic after operation In the first case the leiomyoma was enucleated, leaving the mucous membrane intact Four months later, there were no signs of a diverticulum The pedicled fibromyoma in the second case was removed via the esophageal lumen No relapse had occurred more than four years after operation, and the patient was healthy and able to work

**Ten Year Study of Carcinoma of Esophagus**, reported by Donald P Shedd, Lawrence G Crowley and Gustaf E Lindskog<sup>2</sup> (Yale Univ ), concerns 180 patients Median age was 63 years range 40-86 There were 22 women (12%) Six patients were Negroes The first symptom was dysphagia in 65% and pain was the second most common sign Dysphagia was the chief complaint in 77% Duration of symptoms was less than eight months in most

\* Diagnosis was confirmed histologically in 90% Epidermoid lesions were preponderant, except in the lower reaches, where adenocarcinoma predominated In two, histologic diagnosis was Bowen's disease Histologic diagnosis was obtained by esophagoscopy in 130 cases (70%), by operation in 18 (10%), by postmortem examination in 10 (5.5%) and by other methods in 6 Esophagoscopy and x-ray diagnoses agreed in 36 of 40 lesions in the upper esophagus, in 46 of 52 lesions in the middle segment and in 37 of 40 lesions in the lower esophagus Esophagoscopy was performed in 155 In 139 (89%), diagnosis was positive Most of the lesions for which esophagoscopy was not done or in which diagnosis was negative were in the lower segment A few adenocarcinomas were diagnosed by esophagoscopy In 25 (14%), biopsies of lymph nodes were made, and of these 68% were positive

Exploratory operations were not undertaken in 106, because of distant metastases, local invasion, poor general condition or refusal by the patient On 74 patients (41%) 80 explorations were done, some by more than one approach Resection was performed on 30 patients (38%), 19 for cure and the rest for palliation In 44 patients finding of local

(2) Surg Gynec & Obst 101:55-58 July 1955

invasion was the commonest reason for exploration without resection.

Of upper esophageal lesions (less than 25 cm. from the teeth) 9 were in women and 31 in men. Three lesions were resected, one by the cervical route and the others by trans-thoracic approach. Greatest survival was in patients who had resection. Six of the 30 who had resection died post-operatively, 21 died subsequently and 3 survived. No patient with epidermoid carcinoma lived longer than 27 months and none with anaplastic carcinoma lived over 7 months.

This report provides no reasons for optimism, but if earlier diagnosis can be made, possibly some patients will undergo resection early enough to achieve a cure.

Case Against Segmental Resection for Esophageal Carcinoma is presented by Edward F. Scanlon, Douglas R. Morton, John M. Walker and William L. Watson<sup>3</sup> (Memorial Center for Cancer, New York), with analysis of 79 cases. The determinate positive group consisted of 36 patients (45.6%) with inadequate longitudinal resection, shown by microscopic demonstration of carcinoma at the margin of resection of the surgical specimen, or of recurrent tumor at the line of anastomosis by biopsy or by autopsy. Determinate negative patients, nine in number (11%), definitely did not have recurrence at the line of anastomosis, and surgical margins were clear. The indeterminate group of 34 patients (43.4%) included patients alive and well with no evidence of disease (2 after more than five years), those without microscopic examination of margins of resection or with negative findings and incomplete follow-up, or with symptoms suggestive of local recurrence but without positive biopsy. Of the determinate cases, 80% were considered to have inadequate resection. Probably an even higher percentage would have been obtained if transverse rather than longitudinal sections of margins of resection had been studied.

On the basis of this study, it is apparent that a greater portion of esophagus usually should be removed. Ample margins of normal tissue should be allowed beyond both proximal and distal margins of the cancer. Resection of an

(3) Surg., Gynec & Obst 1



adequate margin of normal tissue on the proximal side with immediate reconstruction can often be done on lesions in the lower third. To provide ample margins for lesions in the proximal and middle thirds, however, subtotal esophagectomy is usually necessary, anastomosis should be done above the clavicle. Even though complete extirpation of the longitudinal extent of the tumor is accomplished, presence of residual disease infiltrating adjacent vital structures will often nullify chance of cure.

To improve survival rate, it is proposed that extensive resection be done as the first part of a two stage procedure. By deferring reconstruction, operating time, blood loss and manipulation of other organs should be reduced, with parallel reduction in operative morbidity and mortality. These benefits could permit a more vigorous attack on transverse as well as longitudinal spread of the tumor by allowing en bloc removal of regional lymphatics and use of new techniques in resection and repair of the tracheobronchial tree and large vessels. A course of radiation therapy could be given in the interval between the two stages. If re-establishment of continuity at the time of resection is considered of major importance, chances of cure are jeopardized unless ample normal tissue is removed beyond the cancer.

► [It seems remarkable that arguments should be presented for a revival of the Torek operation. Yet that is what the authors of this article have done. Can they be right?—Ed.]

**Intrathoracic Transplantation of Right Colon for Esophageal Reconstruction** was performed by Charles D. Sherman, Jr., Earle B. Mahoney, W. Andrew Dale and Samuel J. Stabins<sup>4</sup> (Rochester, N. Y.) in five cases, three cancer, one of tracheoesophageal fistula and one of esophageal atresia. This old method can now be successfully accomplished because of availability of antibiotics to sterilize the colon and because of the great progress in thoracic surgery and anesthesia.

**TECHNIC**—The colon is prepared with neomycin and sulfathiazine.\* Right thoracotomy is used for resection of esophagus in patients with cancer. If necessary, the second part of the procedure can be delayed as a second stage. In patients with tracheoesophageal fistula and delayed reconstruction, definitive thoracotomy is not necessary.

The right colon is mobilized through a longitudinal incision. The

ileocecal artery and all other blood supply except that through the middle colic artery and its marginal artery are occluded. If, after 15 minutes, the cecum is of good color and arteriolar pulsations can be seen, the occluded blood supply is divided, leaving the middle colic artery as the sole blood supply of the transplant. The transverse colon is divided just left of the midline. The terminal ileum is then divided, the distal end turned in and bowel continuity re-established by end-to-end ileotransverse colostomy. The surgeons are divided

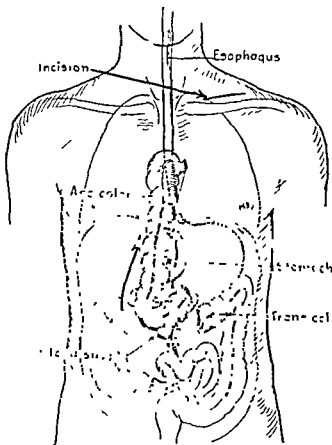


Fig 100—Transplant is swung up anterior or posterior to stomach and through substernal tunnel to neck. (Courtesy of Sherman, C. D., Jr, *et al.*: *Cancer* 8:1198-1205, Nov.-Dec., 1955.)

into two teams, and a retrosternal tunnel is made by blunt and sharp dissection, with one finger dissecting downward from the supra-sternal notch and another upward from the xiphoid, meeting behind the midsternum. The colon transplant is brought up through the sub-sternal tunnel, with care not to twist its blood supply (Fig. 100). If the middle colic artery compresses the pylorus as it crosses anteriorly, it is better to bring the transplant posterior to the stomach. After mobilization of the cervical esophagus and resection of its traumatized stomal end, anastomosis of the end of the esophagus is made, inverting it slightly into the wall of the cecum, with care to make the incision into the cecum parallel to the blood supply entering from

## GENERAL SURGERY

mesenteric border The procedure is completed by anastomosis of the lower end of the colon transplant into the anterior wall of the stomach (Fig 101)

A chest x-ray is taken before the patient leaves the operating room and any pneumothorax removed by needle aspiration If thoracotomy has been done at the same operation, tube drainage is instituted through the right lower chest When the procedure is done in stages,

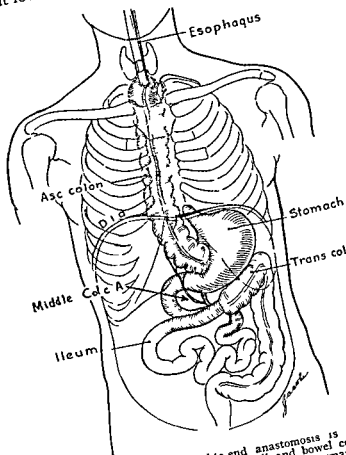


Fig 101—Completed operation end-to-end anastomosis is used in neck end to side anastomosis of colon made into stomach wall and bowel continuity reestablished by end-to-end ileotransverse colostomy (Courtesy of Sherman C D Jr et al Cancer 8 1198 1205 Nov Dec 1955)

it is wise to leave the gastrostomy functioning as precaution against anastomotic complications

One patient who had a one stage resection and reconstruction had a neck fistula on the 12th postoperative day and died of recurrent tumor 4 months after operation Another with carcinoma died suddenly six days after surgery Autopsy, limited to opening the incisions, showed all anastomoses intact Residual tumor was present In the third patient with cancer operation was done in two stages, and later gastroenterostomy was required for pyloric obstruction

tion. He was living and well over a year later. The two children with anomalies had had cervical esophagostomy and gastrostomy at birth two years previously, both were living and well a year after the reconstruction procedure.

Final evaluation of the method must await a larger series and longer follow-up.

**Lower Esophageal Web.** Walter F. Bugden and J. Ernest Delmonico, Jr.<sup>5</sup> (State Univ. of New York, Syracuse) report on two patients with a membranous weblike structure in the lower third of the esophagus treated successfully by surgery. The lesion causes dysphagia, onset of which may be acute or insidious depending on the relative obstructive potential of the food ingested. Meat and bread are most likely to produce symptoms. Once dysphagia begins, the course is likely to be protracted and episodic and finally may become incapacitating.

The lesion is likely to be missed when the esophagus is collapsed. The web is smooth, 3.5 mm thick and produces a constant narrowing, located centrally, thus resulting in a shelflike symmetrical shadow on x-ray. The esophagus above the narrowing is not widened, and proximally peristalsis functions normally. The lesion usually cannot be seen during esophagoscopy.

At thoracotomy the lesion can easily be demonstrated by opening the esophagus longitudinally a few centimeters proximal to the contemplated site of obstruction (Fig. 102) and inserting a finger into the esophagus. Once the web is identified it is intussuscepted upward by the index finger inserted through a gastrotomy incision (Fig. 103). It is difficult to palpate the lesion externally.

In the two patients, obstruction was associated with low substernal discomfort and a sensation of something stuck in the lower chest, often alleviated by drinking water. X-rays revealed a thin web in the lower esophagus, located 3.5 cm proximal to the esophagogastric junction, constant in location and demonstrable only when the esophagus above and below was distended sufficiently to exceed the diameter of the web. The lumen was 3.5 mm. The web was leathery and pliable. The small lumen could barely be felt by the finger tip. The mucosa above and below the defect felt normal.

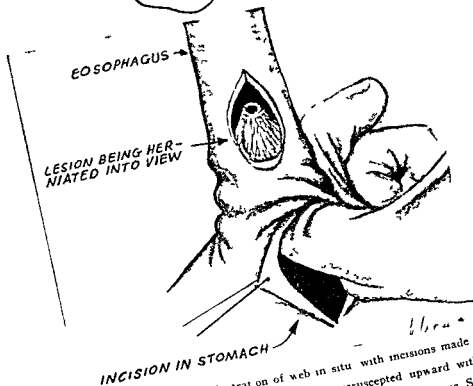
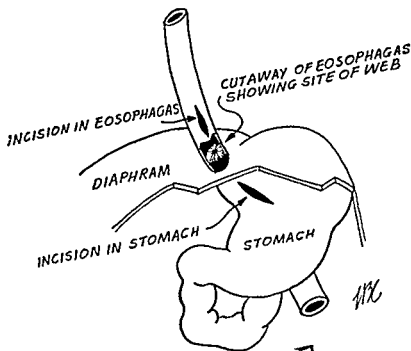


Fig 102 (top) —Schematic illustration of web in situ with incisions made in esophagus and stomach  
 Fig 103 (bottom) —Concept of the web being intussuscepted upward with left index finger in stomach  
 (Courtesy of Bugden W F and Delmonco J E Jr J Thoracic Surg 31 1 18 January 1956)

Three pie-shaped wedges of the membrane were removed, leaving intervening areas of mucosa at the base to prevent subsequent stricture. The raw areas were sutured with interrupted silk sutures, and the incisions in the esophagus and stomach, through which the surgery had been performed, were closed. The patients received liquids orally on the third, and solids before the seventh, postoperative day. They were both completely relieved of dysphagia, being asymptomatic by the seventh and eighth postoperative months.

Pathologically, the surfaces of the lesion were smooth and had the appearance of normal esophageal mucosa. In each, the web was pliable. Microscopically, squamous cell epithelium covered the upper and lower surfaces of the web, and considerable squamous cell hyperplasia, with folding and piling up of the surface epithelium, was noted. Parakeratosis was present in many areas. The submucosa showed considerable chronic inflammatory cellular infiltration, most prominent at the luminal surface. The outer layer consisted of smooth muscle.

Lower esophageal web must be differentiated from esophageal stricture and carcinoma. The web is symmetrical, both circumferentially and longitudinally, whereas the converse is likely to be true in stricture. While the narrowed area relative to a web is likely to be short and thin, a strictured area is usually longer and thicker. Lack of delayed emptying and negative endoscopic findings are present with a web but not with stricture. Cancer can be differentiated by its irregular surface, dilatation proximally, abnormal peristalsis and delayed emptying.

**Surgical Treatment of Bleeding Esophageal Varices.** Experience at Massachusetts General Hospital, reported by Robert R. Linton<sup>6</sup> indicates that many lives can be saved at the time of massive bleeding from esophageal varices by cardioesophageal tamponade with an intragastric balloon, supplemented immediately by transpleural transesophageal suture of varices.

After endotracheal anesthesia (with cyclopropane), with the patient in right lateral decubitus position, the left pleural space is opened by resecting the 7th or 8th rib (Fig. 104). After exposure of esophagus and gastric cardia the balloon

(6) *Wet J Surg* 63:366-377, June 1955

tube (previously inserted for tamponage) is withdrawn. A 5 cm longitudinal incision is made in the esophagus and stomach. Large varices (usually two or three columns) are picked up with their covering mucosa, sutured with a running over-and-over 00 chromic catgut suture carried up the esophagus 4 or 5 cm and down the same distance to include the cardiac mucosa and submucosal veins. The esophagogastric incision is closed transversely with three rows of fine interrupted silk, and diaphragm and thorax are closed.

Among 93 patients with bleeding esophageal varices ad-

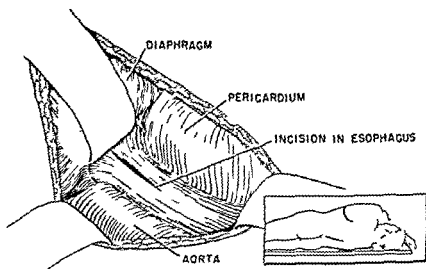


Fig 104—Exposure of esophagus through left thoracotomy incision. Note partial division of diaphragm to expose cardia of stomach and longitudinal incision in lower esophagus and cardia about 5 cm long. Inset shows position of patient on operating table and location of incision. (Courtesy of Linton R R. West J Surg 63:366-377, June 1955.)

mitted in 1946-50 there were no deaths in 28 (30%) with extrahepatic block and satisfactory portacaval shunt was constructed in 23 or 82%. In 65 cirrhotic patients with intrahepatic block shunts were performed in only 33 (51%), the other 32 (49%) died while attempts were being made to prepare them for shunt surgery. During 1951-54, transpleural transesophageal suture of bleeding esophageal varices was performed 24 times in 23 patients, 19 (83%) with intrahepatic and 4 (17%) with extrahepatic block (all post splenectomy bleeders). The lives of four out of five (one with intrahepatic block) for whom the operation was definitive, since shunts could not be constructed, have undoubtedly been prolonged and bleeding episodes reduced. In 12 of the

19 with intrahepatic block, some type of portacaval shunt has been performed, and it is planned in two others. Only one death was directly related to operation; two other patients hemorrhaged again four to six weeks later and died after partial gastrectomy; one died six weeks post suture of hepatic failure. These results contrast favorably with the probable mortality of 60-70% with conservative treatment.

The most effective definitive treatment for bleeding esophageal varices secondary to intrahepatic or extrahepatic portal block is construction of a splenorenal or direct portacaval shunt. Splenectomy with end-to-side splenorenal anastomosis is preferable in most cases. Portacaval shunts should not be performed for ascites alone, but only for bleeding esophageal varices. Splenectomy alone should not be done in a patient with bleeding esophageal varices unless a splenorenal anastomosis can be constructed at the same operation.

Among 116 patients (72, or 62%, males, aged 6-73) subjected to shunt operations up to 1954, 25 (21%) had extrahepatic portal bed block, secondary to Banti's syndrome, and 91 (78%) intrahepatic block secondary to portal cirrhosis. Three who had primary splenorenal anastomoses and one an inferior mesenteric-ovarian venous anastomosis had direct portacaval shunts performed later. There were 79 (66%) end-to-side splenorenal shunts and 36 (30%) direct portacaval anastomoses. Of the 25 with extrahepatic block, 20 (77%) had end-to-side splenorenal anastomoses. Of 94 shunts for intrahepatic block (in 91 patients), 59 (63%) were end-to-side splenorenal and 33 (35%) were direct portacaval anastomoses. Operative mortality was 12.5%. Only 5 deaths occurred in the last 79 shunts (6%). The reduced mortality is attributed to more careful preoperative preparation, including preliminary transesophageal suture of varices in massive bleeders, use of fresh blood transfusions and hypotensive spinal anesthesia, and perfection of surgical technic.

Of 74 patients followed one to seven years after splenorenal or direct portacaval shunt, 66 (90%) were alive, mostly in good health. In a previous series of patients receiving medical treatment, followed one to five years, mortality for extrahepatic block was 10-30% and for intrahepatic block secondary to cirrhosis, 50-80%.



**Management of Corrosive Burns of the Esophagus** is discussed by John Borrie<sup>7</sup> (Univ. of Otago). Severity of the lesion depends on the corrosive swallowed—its chemical nature, concentration, quantity and duration of contact with esophageal tissues. Acids produce coagulation necrosis that limits their action to superficial layers, but alkalis produce a liquefying necrosis, penetrate to the deepest layers and excite an intense inflammation. Lysol produces superficial esophagitis only with no stricture. Severest burns occur in the middle and lower thirds of the esophagus.

The acute phase of local reaction lasts up to two weeks and commences with superficial necrosis and mucosal sloughing followed by inflammatory edema of all layers. In the intermediate phase, the slough separates and passes down the alimentary canal leaving angry red granulations covering a tubular ulcer. Finally, there is gradual replacement by fibrous tissue which contracts to stricture formation. Severity of final stricture is closely related to adequacy of early treatment.

Accurate diagnosis can be made only by esophagoscopy, which should not be delayed even when an obvious oral burn is absent. Fluoroscopy is more important later, in determining the site and nature of subsequent stricture. Chemical strictures, especially in children, are preventable by strictest care with caustic in the home. Though the immediate problem in the acute phase is to neutralize the chemical during the time required to find the antidote, the burn usually has wrought its damage. In the acute and intermediate phases one must relieve symptoms, maintain nutrition, counteract infection and prevent possible stricture by attempting to limit granulation tissue by use of chemotherapy and ACTH and by maintaining the esophageal lumen. In severe cases bouginage is necessary twice daily. If this causes too much discomfort, if speed of stricture formation is too rapid or if the lesion is first seen in the intermediate phase, a wide bore stomach tube should be inserted into the stomach through a cervical esophagostomy to act as an internal esophageal splint and a pathway for feeding.

Many established strictures respond to careful dilatation with bougies. As the stricture dilates, puree should be added.

to the original liquid diet, and finally the patient should eat as much well chewed food as possible. Careful mastication is necessary to avoid temporary episodes of complete dysphagia due to food blocking the narrowed esophageal lumen.

If the stricture does not yield to conservative measures, it must be treated surgically, either by partial esophagotomy and end to end esophageal reconstruction, if it is less than 3 cm long, or by esophagogastrostomy above a longer stricture. Surgical reconstruction in these patients restores not only normal swallowing but a normal way of life.

**Surgical Treatment of Corrosive Stenosis of Thoracic Esophagus by Supra-aortic Esophagogastric Anastomosis without Resection.** Henry P. Limbacher<sup>8</sup> (Tucson, Ariz.) describes a case in a woman 40 followed from ingestion of lye through treatment by dilatation and successful esophagogastric anastomosis, to complete recovery, with later examination of the operative site at autopsy.

**TECHNIC**—With the patient in the right oblique position abdominal incision incorporated a previous left gastrostomy incision. The stomach was mobilized by removing the spleen and transecting the gastocolic ligament and left gastric artery near the celiac axis leaving vessels near the stomach intact as far as possible. Thoracic incision was made from the angle of the 5th rib to the costochondral junction extending inferiorly through costal cartilages to join the abdominal incision. The lung was retracted anteriorly and esophagus freed above the aortic arch; a tube had been placed in the esophagus through the mouth. The lower end of the esophagus was clamped and transected and the normal esophageal opening into stomach was inverted and sutured. After slight mobilization of left lobe of the liver the stomach was brought up for anastomosis with the upper esophagus using an outer row of interrupted cotton and an inner row of continuous catgut sutures. An esophageal tube was passed through the opening into the stomach. After intubation with a small catheter (4 in long) the distal esophagus was inserted into a stab wound in the stomach near the pylorus. A double row of sutures was placed. The stomach was then attached to the posteromedial thoracic wall with interrupted catgut sutures. The diaphragm was closed snugly around the stomach and chest and abdominal walls were closed. Underwater drainage was established through the 9th intercostal space.

The intrapleural tube was removed on the third and the intragastric tube on the sixth postoperative day. The small catheter from the lower esophagus was regurgitated. Soft diet was well tolerated by the 7th postoperative day and the

(8) J Thorac c Surg 29:670-675, June 1955

patient was discharged from the hospital on the 11th day

Postmortem examination 14 months after operation (after a gunshot wound in the head) showed the upper esophago

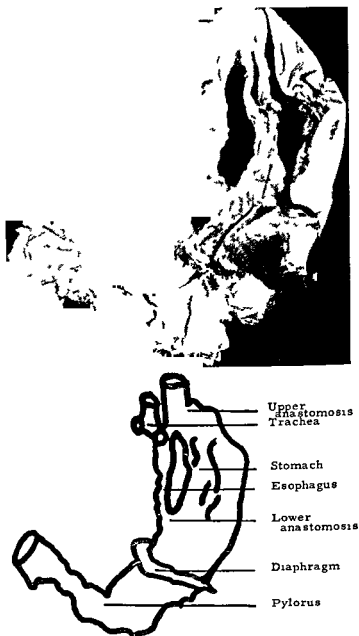


Fig 105 (top) —Postmortem specimen of anastomosis. Aorta has been removed  
 Fig 106 (bottom) —Explanatory diagram  
 (Courtesy of Limbacher H P J Thoracic Surg 29 670 675 June 1955)

gastric anastomosis patent and adequate The lung was normal, with moderate pleural adhesions and adhesions to the stomach The lower esophagus was completely obliterated, so a probe could not be passed from the stomach

to the stenosed esophagus. There was no fluid or debris in the esophagus (Figs. 105 and 106).

Limbacher concludes that supra-aortic esophagogastric anastomosis without esophagectomy offers a satisfactory solution to the difficult problem of esophageal stenosis in selected cases.

---

## THE STOMACH AND DUODENUM

**Familial Occurrence of Congenital Hypertrophic Pyloric Stenosis:** Report of Cases in Siblings and a Cousin and Review of Literature are presented by Angus L. Cameron<sup>9</sup> (Minot, N. D.). Four instances of familial occurrence were observed during 17 years among 68 unselected infants treated surgically. In one instance, the patients were first cousins; in another, three of four brothers were affected.

About 12,000 cases are observed in the United States annually, yet familial occurrence appears to be extremely rare, with fewer than 125 authentic reported cases. Siblings alone are involved in about 75%, usually two male infants, singly born. Only 28 sets of twins have been reported in which both were affected. It remains to be proved that parents who had pyloric stenosis in infancy are more likely to have children with the disease, and in the few recorded instances, coincidence cannot be excluded. If a genetic factor plays a part in development of the disease, there is scarcely any evidence of its occurrence in three generations. Neither is there evidence that parental consanguinity is an etiologic factor.

Available data do not permit evaluation of the genetic factor in the etiology. Therefore, Cameron urges that all familial occurrences be reported in detail for study by medical geneticists and other workers.

**Hypertrophic Pyloric Stenosis: Clinical Analysis of 87 Cases with Special Reference to Etiologic Factors** is made by Don R. Miller and Stanley R. Friesen<sup>1</sup> (Univ. of Kansas). In 87 proved cases of hypertrophic pyloric stenosis, 78% of the patients were males, 89.6% were white, average

(9) A M A Arch Surg 70 877 894, June, 1955.

(1) Am Surgeon 22 108 118, January, 1956

age at onset of symptoms was 2.87 weeks, average age at hospitalization was 5.96 weeks and about a third were first born children, but more were second than first children. Prenatal, birth, family and feeding histories revealed no information of etiologic significance.

All patients had vomiting, which was projectile in 82%. None had evidence of bile or yellow coloration of the vomitus. Other principal symptoms were constipation or decreased number of stools, loss of weight, peristalsis noted by parents and decreased urine output. An abdominal mass was palpable in 80% and was questionably palpable in 7%. Other physical findings were dehydration, abnormal skin turgor and lethargy.

Extramucosal Ramstedt pyloromyotomy was used in all patients. A pyloric tumor was found in all. The lesion was typically olive shaped in all but three patients. One patient had a tumor that was not uniform in circumference, one had aberrant pancreas on the anterior surface of the duodenum and the other had two pyloric rings with a partial duodenal membrane. Tumor sizes ranged from  $1 \times 1$  to  $2 \times 3$  cm. Inadvertent perforation through the mucosa by the myotomy incision occurred in nine patients and was recognized and repaired. No morbidity or mortality resulted from this error.

Postoperative vomiting occurred in 69 patients and was projectile in 1. Reoperation was required, with findings of incompletely divided muscle fibers in the myotomy incision. The average period of postoperative hospitalization was 10.1 days. Two deaths occurred, both on the day of surgery. One patient, a premature infant, died with clinical signs of cyanosis and dyspnea and autopsy showed atelectasis and pneumonitis. The other died of unrecognized hemorrhage from the myotomy site.

In most cases the correct diagnosis can be made by history and physical examination. Barium x-ray studies may be necessary and usually reveal prolonged gastric retention and a "rat tailed" deformity of the pylorus. Fluids and electrolytes must be given parenterally to correct dehydration and electrolyte imbalance. Surgery is performed under general anesthesia through a small right upper quadrant transverse muscle splitting incision. After the tumor is de-

livered into the operative field, the serosa overlying the tumor is incised carefully and the remaining muscle layers spread with a curved hemostat. The mucosa should bulge into the incision. Any bleeding points persisting after a short period of sponge pressure are ligated or sutured. Water is given in small quantities orally 12 hours after operation, then water and formula are given as tolerated. Fluids are given parenterally as needed. Regurgitation of small quantities of feeding is to be expected in the early postoperative period.

**Infantile Hypertrophic Pyloric Stenosis in Parent and Child.** Thomas McKeown and Brian MacMahon<sup>2</sup> (Univ. of Birmingham) traced 112 living patients in whom pyloric stenosis was confirmed by surgery. These patients had 29 children, none of whom had pyloric stenosis. By combining these results with those from two reported series, the incidence of the disease in children of affected parents is estimated as 6.9%. Furthermore, 12 more cases of pyloric stenosis in parent and child were obtained from current records of different hospitals. In 8 of the 12 families the affected parent was the mother. When the results are combined with those of the two published series, there are 33 families, in 17 the mother was affected. Since pyloric stenosis is much more common in males than in females, the risk of the disease is considerably greater in children of affected mothers than in children of affected fathers.

It was also found that the risk of pyloric stenosis is not spread uniformly among all offspring of parents who have had the disease but is highly localized in certain families. Among children in families in which a parent and one child have been affected, the proportion exhibiting the disease is about 40%.

Several features of pyloric stenosis are incompatible with sex-linked inheritance, and the sex difference in incidence must presumably be attributed to genetic processes whose nature cannot be specified. In this respect, pyloric stenosis is characteristic of a class of diseases (e.g., peptic ulcer) in which susceptibility is different in the two sexes, but is certainly not due to a single gene.

**Surgical Management of Massive Acute Upper Gastrointestinal Hemorrhage** from ulcer, recommended by Claude E Welch, Arthur W Allen and Gordon A Donaldson<sup>3</sup> (Boston), is based on an analysis of all cases observed at Massachusetts General Hospital from 1923 through 1953. A death rate of 13% early in this period increased to 17% in 269 patients treated during 1948-53. The rise is attributed chiefly to the increasing age of the patients and to postoperative complications. Mortality of all patients with massive hemorrhage, treated medically or surgically, is 7% for those under 50 years, 13%, 50-59, 25%, 60-69, and 29% for 70 and over.

Elderly patients appeared to tolerate early surgery better than expectant treatment. The mortality of 17 patients over 80 was 35%. Medical therapy alone was successful in 6 of 14, but in 3 of these, no cause of hemorrhage was found by x-ray. Of 11 with demonstrated lesions, medical therapy failed in 8 (73%), who had further hemorrhage leading to long delayed surgery in 3 and to death in 4 without surgery. One patient survived a second massive hemorrhage a few months later. Three patients who had surgery within 24 hours of admission survived.

Prevention of postoperative complications and earlier surgery on patients with massive hemorrhage who are over 60 should lower mortality. Recommended emergency operation is distal removal of about 75% of the stomach, preferably including removal of the ulcer. At times, it may be safer to divide the duodenum proximal to the ulcer, with secondary operation later, if required. Double jejunostomy tubes are usually inserted.

To avoid pulmonary complications, the most important cause of postoperative death, aspiration during operation is avoided, the stomach is kept empty during the early postoperative period, decompression is carried out, either with a Levin tube or preferably a retrograde catheter through the efferent jejunostomy loop, and the use of antibiotics, started before surgery, is continued for five days after operation. To prevent pulmonary emboli, early operations, routine use of elastic stockings, postoperative leg exercise, early ambulation and avoidance of tight abdominal binders are important. Prophylactic anticoagulants are sometimes used,

and if thrombophlebitis or pulmonary infarct occurs, interruption of femoral veins is carried out. Early and speedy operations are important in the control of postoperative shock. If bleeding recurs early after ulcer has been excluded rather than resected, secondary resection should be done.

Application of these principles in 55 consecutive private patients (included in total series), operated on personally, resulted in 53 recoveries. Two patients who had had previous perforations died after two stage gastrectomies, one of a bleeding anastomotic ulcer, the other of a perforated gallbladder. Prompter operations and better postoperative nursing probably account for better results among private patients.

**Surgical Significance of Gastrointestinal Bleeding.** Carleton Mathewson, Jr., and Benjamin Sugar<sup>4</sup> (San Francisco) state that bleeding peptic ulcer and esophageal varices are the main causes of serious gastrointestinal bleeding. Massive gastrointestinal bleeding is that amount sufficient to cause sudden weakness, dizziness or syncope, often almost immediately followed by vomiting of a large amount of blood, passage of a large tarry stool, or both. The victim is pale, cold and sweating, slightly cyanotic, restless and thirsty. The pulse is small and rapid, usually over 120/minute, and the systolic pressure generally below 90. The cause of gastrointestinal bleeding is often difficult to diagnose. Gastric, duodenal or anastomotic ulcers are responsible for half of the gross hemorrhages from the upper gastrointestinal tract. Other lesions are esophageal varices, gastric neoplasms, acute gastritis, benign tumors and aneurysms. Fatal hemorrhage usually originates from esophageal varices or from erosion of a large artery, usually the superior pancreaticoduodenal, the right or left gastric or their major branches. Persistent slow bleeding usually comes from erosion of smaller vessels in the submucosal plexus.

Prognosis is difficult to determine. The mortality risk of hemorrhage from ulcer increases with age of the patient. There is a definite correlation between arteriosclerosis and bleeding. Gastric hemorrhage has a higher mortality than duodenal ulcer hemorrhage because the former nearly always is due to erosion of the right or left gastric ar.

(4) Am J Surg 89 1177 1181 June 1955



whereas bleeding from the duodenum frequently is from small submucosal vessels. Exact determination of duration of bleeding, though difficult, is of grave prognostic significance.

Every patient with gastrointestinal bleeding must be seen immediately by an internist and a surgeon. Blood studies are made to rule out primary blood diseases and a slow drip transfusion is started immediately. The pulse rate and blood pressure, the best indices to continued or recurrent bleeding, are recorded every 15 minutes. Pulse rate should be less than 90/minute and systolic pressure above 100. The hemoglobin and hematocrit values are determined. Signs of pallor, restlessness and sweating are important evidence of bleeding. Morphine can be given in small amounts. An indwelling Levin tube is helpful in removing clots. The patient should not be fed. Stabilization nearly always occurs with two or three 500 cc transfusions of whole blood. Sweating about the head is an early sign of renewed bleeding. Failure to respond to whole blood transfusions is the major indication for early surgical intervention. If stabilization occurs and sudden bleeding recurs, blood replacement is carried on rapidly and surgery advised. When stabilization can be maintained with intermittent blood transfusions conservative management is continued. Interval resection may be considered later.

Before surgery a nasogastric tube is inserted and the stomach evacuated. Intratracheal anesthesia is best. Open inspection of the stomach and duodenum, control of hemorrhage with pressure, and restoration of blood pressure with rapid transfusion before further manipulation within the abdomen are the three most important maneuvers at the time of surgery. After blood pressure is restored, an elective procedure can be performed. The operation of choice for chronic peptic ulcer is partial gastrectomy. Duodenal ulcers may or may not be removed, depending on local circumstances.

Of 215 patients with massive gastrointestinal bleeding seen in 1947-52, 33% died. Diagnosis was peptic ulcer in 97, with 64 duodenal, 27 gastric and 6 marginal. The mortality rate in the ulcer patients was 12.3%. Esophageal ulcers were found in 67 and 66.3% died. The source of

bleeding was not determined in 47, of whom 27.7% died. Of 21 patients operated on during the acute stage of bleeding, 1 died of a myocardial infarct. Surgery was lifesaving in most patients.

**Massive Gastrointestinal Hemorrhage** is discussed by C. F. W. Illingworth<sup>5</sup> (Univ. of Glasgow). Gastrointestinal blood loss is usually greater than apparent from hematemesis or melena. With the possible exception of bleeding from esophageal varices, the vomit represents only a small part of the total. Most of the blood loss remains concealed within the abdomen, and three or four pints may be hidden in the dilated stomach and in coils of small and large intestine. The clinical evidence tends to underestimate the blood loss. In a healthy adult, as much as two pints of blood can be lost without acceleration of the pulse and with no decrease in blood pressure. Routine blood examinations fail to give accurate index of blood loss. The main danger of massive hemorrhage is not from immediate exsanguination but from prolonged anoxia. Few patients die of acute hemorrhage. Most die, after several days of continuous or recurrent oozing, of cerebral impairment, renal ischemia, myocardial damage and similar results of faulty oxygenation. Essential treatment of massive gastrointestinal hemorrhage is rapid and full replacement of lost blood.

Hemorrhage from the alimentary tract may arise from a multitude of lesions, ranging from swollen gums to hemorrhoids. In hematemesis, only esophageal varices, gastric and duodenal ulcer and various acute lesions of the stomach need be considered. In melena without hematemesis, tumors and ulcers of the small intestine must be included. Practically, it is only necessary to distinguish esophageal varices from the other lesions. A history of hepatitis or alcoholism and findings of spider nevi, liver enlargement, ascites or splenomegaly aid in the diagnosis. Barium swallow may be necessary to outline the varices or demonstrate a peptic ulcer. Patients with exsanguination due to esophageal varices are usually not candidates for major surgery and should be treated by balloon tamponade, whereby one balloon is placed in the lower end of the esophagus and another in the cardia end of the stomach. The tam-

(5) Ann. Roy. Coll. Surgeons England 16:337-341, May 1955.

ponage can be used only for one or two days but gives time for restoration of blood volume should major surgery be necessary

Chronic peptic ulcer is the commonest cause of massive hemorrhage from the stomach and duodenum Acute gastritis is another cause Treatment includes rest, morphine intravenously for sedation and—most important—prompt and adequate blood transfusion The amount required is rarely less than 3, and may be 8-10 pt Gastric lavage and tube feedings with a milk drip are valuable

Surgical treatment is rarely required for initial hemorrhage, which usually undergoes spontaneous arrest, but is mainly indicated for continued or recurrent bleeding Patients who do not improve after 24-36 hours may be candidates for surgery Age, though significant, is not the most important factor in surgical treatment

Gastrectomy should be done for gastric ulcers Duodenal ulcers are more difficult to treat Ligation of the gastroduodenal artery and stitching of the bleeding point are not always successful Proximal gastrectomy may be done and the duodenum stump enfolded to exert direct pressure on the point of bleeding If the bleeding source cannot be found, gastrectomy should be done without first opening the stomach During the course of the gastrectomy, the stomach and duodenum should be carefully inspected

► [Illingworth's extensive experience with this condition adds great value to his recommendations—Ed]

**Problem of Bleeding Peptic Ulcer** J Garrott Allen and Harry A Oberhelman, Jr<sup>6</sup> (Univ of Chicago) believe that the causes of death from bleeding peptic ulcer are exsanguinating hemorrhage, bronchopneumonia due to aspiration, renal failure from prolonged shock or mismatched blood transfusions, and cardiovascular accidents and pulmonary embolism in older patients A gastric ulcer erodes into the left gastric artery, a duodenal ulcer, into the gastroduodenal artery Most bleeding ulcers are on the posterior aspect of the stomach and duodenum A perforating ulcer into the peritoneal cavity is seldom the site of massive hemorrhage The anterior aspect of the stomach and duodenum, where most of the perforations occur, contains few large arteries Scar tissue in the ulcer bed and arteriosclerotic

blood vessels favor continued bleeding or its intermittent but frequent recurrence.

Massive bleeding from peptic ulcer is a self-evident symptom. Esophageal and gastric varices account for 5-10% of the patients with massive hemorrhage. Gastritis, esophagitis, venous telangiectasia of the gastric mucosa, benign and malignant tumors, blood dyscrasias and other causes, combined, account for less than 10% of the bleeding. Whether diagnostic tests can be done depends on the patient's condition. If surgical intervention is not imminently necessary, gastric suction should be instituted for 24 hours to remove the contents of the stomach and to reduce the quantity of gastric juice remaining in the stomach. If the patient's condition permits, gastroduodenal fluoroscopy may be performed. Some physicians have advocated gastroscopy. Many surgeons prefer to intervene surgically without the fluoroscopy, since the lesions can easily be seen by direct inspection.

The patient should have a normal pulse rate and arterial blood pressure before surgery is done. The continued administration of blood is the most important preoperative factor. Laboratory procedures include red cell count, hemoglobin concentration and hematocrit.

The goal in the surgical management is hemostasis, and the best operation for this is subtotal gastric resection. This procedure removes the bleeding gastric ulcer but not necessarily the bleeding duodenal ulcer. The latter must be excised or excluded with the bleeding point sutured. In either case, the duodenum and the remaining gastric segment should be opened and inspected, since two ulcers may be present. Less extensive surgical procedures are not satisfactory. High gastric resection for massive hematemesis is also the emergency surgical treatment for gastrotaxis, gastric and esophageal varices, or tumor. If an emergency exploration is indicated for massive hematemesis, "blind" subtotal gastrectomy needs no apology if the decision to operate was correct in the first place.

The decision to operate on the patient with a bleeding peptic ulcer is contingent on several factors. The most important is failure to respond to supportive therapy; others include the facilities available, amount of blood available,

duration of bleeding, age of the patient, other diseases and whether bleeding has occurred previously. There are no rules of thumb, each patient must be judged individually.

**Duodenal-Ulcer Family** (the K family) is described by J. T. Wright, Alan Grant and Denys Jennings<sup>7</sup> (London Hosp.), in which 9 of 13 living siblings have duodenal ulcers (Fig 107). In two there was some evidence of past ulceration, and in only two was the duodenal cap normal on x-ray. One of these last had "giant" gastritis. Of four cousins (J family), two have duodenal ulcers. There appeared to be no environmental factor to explain why some members of the K family had more trouble than others. They were all

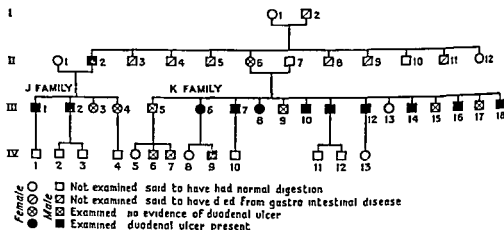


Fig 107—Families K and J (Courtesy of Wright J. T. *et al.* Lancet 2 1314 1318 Dec 24 1955)

brought up under conditions of hardship and financial stress. All the men have smoked heavily, but the two without ulcers are the heaviest smokers and two sisters with ulcers have never smoked. Two who stopped smoking, however, had considerable symptomatic relief. Five brothers admitted to fairly heavy alcohol consumption at some time, two have ulcers, two do not and one may have had an ulcer. In only one case did ulcer symptoms appear in the year of marriage, but in five there was some association of symptoms with a change in occupation. No search was made for deep psychologic causes. Except for one member of the fourth generation the family seems essentially normal.

All members of the K family belong to blood group O; two affected members of the J family belong to group B.

Nearly all members of the K family are "nontasters" of phenylthiourea, and the only one who is an unequivocal "taster" has no duodenal ulcer.

Roentgen appearance, particularly the outline of the stomach and splenic flexure of the colon, was much the same in all K siblings. The shape of the duodenal cap varied widely, but in two sisters there was an identical hooklike projection at the base of the cap on the side of the lesser curve, and two male cousins had a lesser degree of the same deformity. In several cases the duodenal loop was relatively small and the third part of the duodenum, which lay behind the cap, tended to remain filled with barium.

Role of Pyloric Antrum in Experimentally Induced Peptic Ulceration in Dogs was studied by David State, Alfred Katz, Robert S. Kaplan, Bernard Herman, Leon Morgenshtern and Irving A. Knight<sup>8</sup> (Univ. of Southern California). Of 14 control dogs in which a 50% resection of the acid-secreting portion of the stomach was done, with restoration of gastrointestinal continuity by a Billroth I or II procedure (short loop posterior gastroenterostomy), 9 developed ulcers after daily intramuscular injections of 30 mg. histamine base in beeswax. Ulcers developed in 2 of 16 dogs in which a "sleeve" resection with removal of 50% of the acid-secreting area and anastomosis of the residual gastric pouch to the antrum, was performed. Of 15 dogs with a 50% "pie" or "wedge" resection, leaving the lesser curvature intact, 1 developed an ulcer. Four dogs with "sleeve" and five with "wedge" resections that failed to show histamine induced ulcer after 30 days were reoperated on, their antrums were resected and gastrointestinal continuity was restored by Billroth I or II technic. In eight of these nine, ulcers developed after they again received histamine for 30 days. The amount of residual and secreting gastric mucosa remained the same before and after antral resection.

These results and findings by others indicate that when the antrum is in continuity with the acid secreting portion of the stomach as secretion of gastric juice increases, inhibition by antral function comes into play. Whether this inhibition is a specific function of the antrum, and if so whether it is due to decreased formation of gastrin or to

liberation of a specific gastric inhibiting hormone, is not known

The 10% incidence of histamine-induced ulceration after 50% "sleeve" or "wedge" gastric resection in dogs precludes its acceptance in man as a suitable operation for peptic ulceration. Wagensteen reported on 90 patients with 85% resections of "sleeve" or "wedge" type without recurrent stomal ulceration. The authors used a similar technique in 26 patients removing approximately 75% of the acid secreting mucosa with no fatalities and no recurrent ulceration. Longest follow-up, however, is only two years. It appears that incidence of "dumping" is decidedly less than after a Billroth II procedure, although not entirely eliminated. Weight gain after operation has been better than after the Billroth II procedure.

**Study of Serum Amylase Concentration in Patients with Acute Perforation of Gastroduodenal Ulcers.** Value of serum amylase determination in diagnosis of acute pancreatitis is universally recognized, but other acute intra abdominal diseases may produce perhaps indirectly, elevation of this enzyme. These diseases include perforations of the upper gastrointestinal tract, acute cholecystitis, common duct stone, strangulated intestinal obstruction and appendical peritonitis.

J. Herman Mahaffey, H. Leroy Brockman, George L. Jordan Jr., and John M. Howard<sup>9</sup> (Houston) report results of preoperative serum amylase determinations in 51 patients with acute perforations of gastroduodenal or marginal ulcers. In 70 normal controls, normal range was 15-50 units. Eight patients (15.7%) had distinct elevation of serum amylase values and three others had values of 52, 53 and 53. Only 1 of 22 patients admitted less than six hours after perforation had increased serum amylase levels. Most significant elevations were seen when perforation occurred 12 or more hours before admission. Of 19 patients seen late after perforation, 26% had amylase concentrations of 94-220 units.

Only two (7.4%) patients with perforations less than 1 cm. in diameter had increased serum amylase levels, but all three patients with perforation over 1 cm. had a distinct elevation. Only 1 (5.3%) of 19 patients with intraperitoneal

spillage of gastroduodenal contents estimated at less than 600 ml. had elevated amylase levels, whereas 30% of 20 patients with greater spillage had a significant rise. Amylase concentration was elevated only in patients who had ingested food or alcohol within three hours before perforation.

Though highest serum amylase concentrations were found more than 12 hours after perforation, in contrast to findings in acute pancreatitis, this diagnostic distinction is not reliable because occasionally a late rise in amylase levels is noted in patients with acute perforation demonstrated of the authors' patients with acute pancreatitis, and one a rise within 6 hours. Consequently, serum amylase levels cannot be relied on for absolute differentiation between these two conditions but must be interpreted with clinical findings. An upright x-ray of the abdomen, demonstrating free air under the diaphragm, was of considerable diagnostic aid in several patients with high serum amylase concentrations.

**Nonoperative Treatment of Perforated Peptic Ulcer:** Further Report is given by Sam. F. Seeley and Donald Campbell (Walter Reed Army Med. Center). Nonoperative therapy of this condition is based on the premise that a perforation will close itself provided the stomach is kept empty so that nothing passes through the opening and the patient is given adequate supportive treatment.

A definite clinical diagnosis of perforated peptic ulcer was made in 136 males and 3 females, of whom over half were under age 40, 23% were over 50 and 2 were over 70. In 97.8% the clinical diagnosis was confirmed by demonstration of free air in the peritoneal cavity, positive findings in the convalescent gastrointestinal x-ray series or, in patients who came to elective surgery for chronic ulcer, operative demonstration of the sealed ulcer. The site of perforation was the duodenum in 134 and the stomach in 5. In 11 there was a definite history of previous perforation. Concurrent hemorrhage was observed in two. In 115 cases treatment was instituted less than 12 hours after perforation.

There were seven deaths, an over-all mortality of 5%. Excluding five patients who were inoperable when first seen, 2 died among 134, a corrected mortality rate of 1.5%. This figure is well below the average mortality rate of 8.7%

(1) Surg., Gynec. & Obst. 102 435 446, May, 1956



## GENERAL SURGERY

in 12 operative series Excluding the seven deaths, there were 27 complications in 24 patients The major complications were subphrenic abscess in seven, pleural effusion and pneumonia in four each, pelvic abscess and drug psychosis in two each and penicillin reaction, thrombophlebitis and pyloric stenosis in one each These figures compare favorably with those of many operative series when complications secondary to the wound are excluded

Treatment consists in inserting a Levin tube into the stomach immediately and aspirating the contents The patient is placed on his left side and a left lateral decubitus x-ray taken Continuous gastric decompression is maintained and morphine and fluids are given intravenously No oral fluids or feedings are allowed The patency of the Levin tube is tested by gentle instillations of normal saline solution and its withdrawal at frequent intervals During the first 24 hours, 3,000 cc of fluids is given intravenously Parenteral administration of vitamins is included Every 12 hours until the 5th day, the patient is given an intravenous solution containing 1,000,000 units of penicillin, 1 Gm streptomycin and 25 Gm sodium sulfadiazine in 1,000 cc normal saline solution or 5% glucose in water

Rigidity of the abdomen usually disappears within 12 hours, regression being from below upward, and always in 36-48 hours Deep tenderness usually persists in the epigastrium up to the sixth day Peristalsis may be elicited on the second or third day On the fifth or sixth day a mixture of equal parts of milk and cream is given in 30 cc portions orally each hour with the nasogastric tube in place but not with suction If no evidence of peritoneal irritation occurs during 24 hours of this regimen, the tube is withdrawn and the diet gradually increased Ambulation is allowed when the Levin tube is removed Streptomycin and sulfadiazine are usually discontinued on the 5th day, but penicillin is given intramuscularly until about the 10th day By the 14th day the patient can be discharged on a regular ulcer diet and can then have an upper gastrointestinal series Although careful follow up was not carried out in this series, in 14 patients subsequently operated on for cure of chronic ulcer there were minimal peritoneal adhesions and no fluid or foreign material in the peritoneal cavity

Theoretic criticisms of the nonoperative method are that (1) aspiration will not be successful when perforation occurs with a stomach filled with food or liquid, (2) it is difficult to guess which lesions will seal spontaneously, (3) there is danger of passing the aspiration tube through the perforation, (4) there is often insufficient evidence of diagnosis in successful cases, (5) the diagnosis may be missed in cases of acute perforative appendicitis, cholecystitis, diverticulitis and in cases of devitalized bowel, (6) perforations due to malignancies cannot be distinguished, and (7) the necessary period of bed rest increases the chances of fatal complications. The most obvious advantage of nonoperative treatment is lower mortality and morbidity. Operative risk and complications, especially in misdiagnosed cases in which operation is contraindicated, are avoided and convalescence is usually shorter and more comfortable.

► [It seems remarkable that results like this can be obtained without operation. Of course they are due not only to keeping the stomach empty but also to better understanding of the use of fluids and electrolytes as well as the newer drugs with which to prevent infection.—Ed.]

**Simple Suture in Treatment of Perforated Gastroduodenal Ulcer** is recommended in most cases by A. G. Weiss, L. Hollender and E. Schvingt<sup>2</sup> (Strasbourg), although they emphasize that no single method should be applied routinely. In 97 cases in which a perforated ulcer was sutured, no deaths occurred in 92 seen within 16 hours, although postoperative complications—half of them pulmonary—occurred in 12 of these. Time between perforation and suture in five fatal cases was 16–24 hours. One had postoperative pyloric stenosis and failed to survive gastroenterostomy performed the 11th day after suture. Four deaths occurred in poor risk patients. Peritonitis was the cause in one with alcoholic cirrhosis and one with obesity and asthma. Shock and heart failure in one confined to a mental hospital for 15 years, and pneumonia in one who had had chronic bronchitis for many years. Cicatricial hernias occurred in 14, but after subumbilical median incisions and chromic catgut were replaced by right transrectal incisions and closure in three layers with Nylon—no parietal complications occurred.

Follow up of 82 patients 18 months to 7 years after suture revealed that 26 (31.7%) had had no further surgery. Twelve of these were completely well but followed a spe-

(2) J. *hon. chir.* 50:431–444, May/June 1955.

cial diet Nine required medical treatment and had occasional mild symptoms Three had intermittent pain and two almost constant symptoms for which operation was contemplated Secondary gastrectomies were performed in 56 (68.2%) for persistent pain in 41, repeated hemorrhages in 8 massive hemorrhages in 4 and recurrent perforations in 3 Two deaths followed these secondary gastrectomies, one from massive pulmonary embolism and one from hemorrhage due to loosening of an arterial suture

The authors believe that direct suture is the safest procedure in perforated duodenal ulcer because it permits cleansing of the peritoneal cavity and correction of any diagnostic errors After opening the abdomen immediate gastrectomy may be performed if local conditions and the patient's general state are favorable In general, suture is more logical than continuous suction, which is too hazardous for routine use

**New Physiologic Concepts Related to Surgical Treatment of Duodenal Ulcer by Vagotomy and Gastroenterostomy** are reported by Harry A Oberhelman, Jr, and Lester R Dragstedt<sup>3</sup> (Univ of Chicago) From 1943 to 1953, 487 patients with duodenal ulcer were treated by vagotomy and gastroenterostomy, with good results in 400 (82%), fair in 38 (8%) and poor in 49 (10%) Marginal gastrojejunal ulcer developed in 28 of the last group, 8 of whom showed persistent reduction in the 12 hour nocturnal gastric secretion so it may be assumed that vagotomy was physiologically complete and the nervous phase of gastric secretion completely abolished In these eight patients gastroenterostomy stomas had been placed either opposite the incisura or at the midfundus of the stomach, and preoperative stenosis which produced moderate to high grade obstruction was present in all Cicatricial pyloric stenosis often increases as the ulcer heals and in many of these patients little barium could be forced through the pylorus after vagotomy and gastroenterostomy

Most of these patients had been operated on early in the series when no special attention was directed toward positioning the gastroenterostomy stoma near the pylorus After 1952 following physiologic observations in experimental animals showing that high lying gastroenterostomy

(3) Surg Gynec & Obst 101:194-200 August 1955

produces stimulation of gastric secretion, which does not occur if gastroenterostomy stoma is located in the antrum or near the pylorus, this was taken into account in performing the operation

In 11 of the 28 patients with marginal ulcers after operation, little or no reduction in 12 hour nocturnal gastric secretion, occurred, and all showed positive response to insulin hypoglycemia. Poor results in these patients may probably be accounted for chiefly by incomplete vagotomy though high lying gastroenterostomy may have been contributory. In nine patients with proved recurrence, secretory data were insufficient to permit analysis

In 2 of 487 patients benign gastric ulcer subsequently developed one and seven years after original operation. Severe antrum gastritis developed in two, two and three years after surgery. Secretory studies in these four patients indicated that vagotomy had been complete and the nervous phase of gastric secretion abolished. These failures probably were also due to stasis of food in the stomach, resulting from decreased motility and high lying gastroenterostomy

Experimental and clinical evidence indicates that the stoma should be placed in the antrum within 4 or 5 cm of the pylorus whenever gastroenterostomy is done with vagotomy

Results of Ulcer Surgery performed at the University Clinic in Vienna, 1948-53, are reported by G. Hienert.<sup>4</sup> During these six years, 1,231 patients with peptic ulcer were hospitalized, but operation was contraindicated for various reasons in 143. Resections were performed in 976, with 44 deaths (4.5%), 950 of these were two thirds resections (Billroth II) with anastomosis of the entire stomach remnant with the short upper jejunal loop. Mortality in this group of resections was 4.5%, 0.5% less than in a series reported by Huber from the same clinic for the years 1923-39. Vagus resection was done in 16, gastroenterostomy in 7 (two deaths) and exploratory laparotomy in 1. Mortality for these 1,000 cases without perforation or recurrent ulcers was 4.6% representing improvement over Huber's series of 0.9%

In addition, there were 13 operations for recurrent jejunal

(4) Wien klin Wchnschr 68:339-341 Apr 27 1956

## GENERAL SURGERY

ulcer, with one death from pulmonary complications 17 resections for perforated ulcer, with one death from massive embolism and 48 sutured perforations, with seven deaths. Primary resection of perforated ulcer carries no greater mortality risk than resection of uncomplicated ulcer. As a result of antibiotics, sulfonamides, transfusions, etc., the mortality in perforated ulcer has been reduced from 24 to 12.3%.

Follow up of 80% of this series of surgical patients showed that 90% are symptom free and able to work although a few cannot tolerate certain foods.

The over-all mortality of 5.1% is consistent with the reported average. In a reported series of 1780 ulcer cases in which operation was not performed death resulted in 17.5% (about 10%). Hence surgical risk to life is considerably less than that of the ulcer itself, and gain in health after operation is, as a rule, striking.

**Suture Control of Bleeding Duodenal Ulcer Safer Approach in Treatment of Critically Ill Patient** is recommended by Hollis L. Albright and Richard C. Kerr<sup>5</sup> (Brookline Mass.). Recently there has been increasing acceptance of emergency surgical treatment for patients with uncontrollable (by transfusions and conservative medical management) massive hemorrhage from peptic ulcer. Enthusiasm has centered principally around the performance of subtotal gastrectomy. However, this group of patients constitutes the greatest operative hazard. That subtotal gastrectomy may be the desirable definitive treatment for the patient's ulcer should not be considered at all in emergency care. Even expert and rapid subtotal gastrectomy adds unjustifiable risks of prolonged anesthesia and major resection without offering a better chance of control of bleeding than does simple bleeding point suture. It may offer less chance of bleeding control if the ulcer cannot be excised with the specimen and if blind gastrectomy is performed. Listed causes of death following this procedure show that recurrent bleeding from the ulcer is one of the most frequently mentioned conditions. Duodenotomy or gastrotomy with ready transection of the pylorus, generous exposure of the ulcer, direct suture control of the bleeding point—

and no further surgery—constitutes the safest possible treatment for these gravely ill persons

In six of seven patients treated by simple suture, blood pressure immediately returned to normal and no further bleeding occurred. There was one fatality, in an extremely poor risk patient, aged 67, whose blood pressure had been almost constantly at shock levels for four days following a massive hemorrhage. It was believed that surgery offered him his only chance and a bleeding vessel at the base of a duodenal ulcer was ligated. Bleeding recurred two days later, with shock, and he died on the sixth postoperative day. The six surviving patients have resumed normal activities, four having had definitive surgery later. Two have gone 9 and 14 months without further bleeding.

Adequate direct suture of the bleeding ulcer is a satisfactory method of stopping blood loss, the sole requirement of emergency surgery in these cases. Gastrojejunostomy is not needed, pyloric obstruction being prevented by transverse closure of the pyloric portion of the longitudinal visceral incision. This method is much safer than subtotal gastrectomy with or without excision of the ulcer and deserves further trial.

**Simplified Technic Using Chymotrypsin Lavage for Cytologic Diagnosis of Gastric Cancer.** Cyrus E. Rubin and Earl P. Benditt<sup>6</sup> (Univ. of Chicago) describe a technic for chymotrypsin lavage of the stomach for detection of cancer that is simple, effective, safe, causes the patient minimal discomfort and is not time consuming.

**TECHNIC**—After an overnight fast (drinking of water is urged), a Levin tube is passed into the stomach with glycerin or water used for lubrication. The fasting stomach is aspirated and the fluid centrifuged. A preparatory lavage with Ringer's solution ensures a clean empty stomach. Repeated 100 cc quantities are instilled until the return is clear, the patient being turned through 360 degrees to ensure washing of the entire stomach. The aspirate is centrifuged, smeared and fixed. The enzyme lavage solution is prepared by adding 7 mg crystallized alpha chymotrypsin to 500 cc of 0.1 M acetate buffer and the solution instilled into the stomach. Most patients tolerate 500 cc; some need only 300 cc. After 10 minutes (no longer) the solution is reaspirated as quickly as possible. The last few drops may yield the best specimen and should be smeared on separate slides. They are obtained with the first to second mark (45-55 cm) of the Levin tube at the level of the teeth and with the patient in both

(6) *Cancer* 8:1137-1141, Nov-Dec, 1955

and left lateral decubitus positions. While sufficient fluid is being collected to fill the centrifuge, the filled tubes should be placed in an ice bath to slow enzymatic digestion. A portable angle head centrifuge (10-50 cc plastic cups, 5,000 rpm for three minutes) should be used at the bedside to process the whole 500 cc immediately. Blood in the aspirate does not interfere with results.

The smears are immersed while wet in a fixative composed of equal parts of ether and 95% ethyl alcohol. A half hour is required for fixation, but the slides may be stored unstained in a fixative for weeks in the refrigerator provided ether is added at intervals as it evaporates. They are then gently moved through 22 successive dishes of solvent and stain according to the Papanicolaou method.

A group of 64 patients with possible gastric cancer were examined by the method. Of the 20 who proved to have cancer, 19 were detected by the chymotrypsin lavage. The evidence suggests that this method yields numerous diagnostic cells excellently preserved.

**Cytologic Diagnosis of Gastric Cancer by Chymotrypsin Lavage**—*I Accuracy of method*—Melvin I Klayman, Barbara W Massey, Sylvia Pleticka, John T Galambos, Lloyd Brandborg, Joseph B Kirsner and Walter L Palmer<sup>7</sup> (Univ of Chicago) report on 313 symptomatic patients examined for gastric malignancy by the chymotrypsin lavage cytologic method.

**TECHNIC**—Patients are prepared by an overnight fast and urged to drink water before the test. The stomach is cleansed by irrigation with Ringer's solution through a Levin tube. The gastric aspirate is centrifuged and one pair of slides is made from the sediment. Acetate buffer (pH 5.6), 500 cc with 7 mg salt-free chymotrypsin is instilled into the stomach. The patient lies down and rotates through the four positions of the right side, supine, left side and prone for two minutes each. The aspirate is collected in 50 cc plastic tubes packed in ice and centrifuged immediately for three minutes at 5,000 rpm. Two pairs of slides are made from the sediment fixed immediately in ether-alcohol and stained.

Of 75 proved malignancies, 60 were identified correctly. Failures were due to reader's errors, superficial fibrin membrane on the malignancy or complete esophageal obstruction in 6 patients; the cause of failure was not apparent in the other 10. Among 78 patients proved free from malignancy, diagnosis was negative in 76, inconclusive in 1 and incorrectly positive in 1. Clinical observation carried out in 160 patients for 6-21 months after results of cytologic examination were negative in 157 and positive in 3; the subsequent studies and clinical course of the 157 patients corroborated

(<sup>7</sup>) *Gastroenterology* 29:849-862 November 1955

the negative results and suggested that the positive results were false. Combined use of x-ray, endoscopy and cytologic methods correctly diagnosed 69 of 75 gastric neoplasms dur-

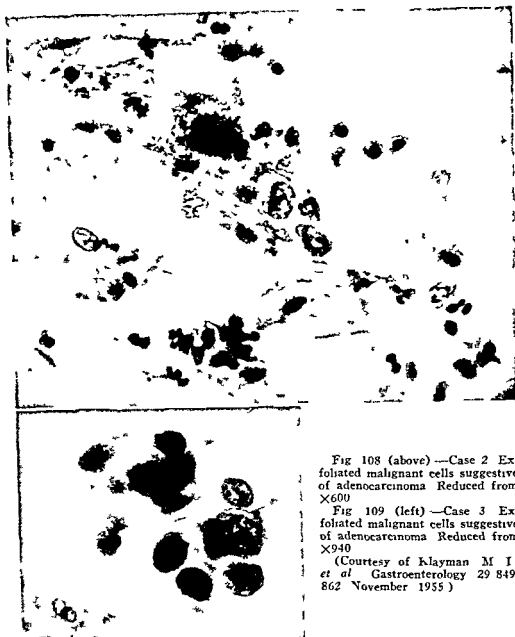


Fig 108 (above) —Case 2 Exfoliated malignant cells suggestive of adenocarcinoma. Reduced from  $\times 600$

Fig 109 (left) —Case 3 Exfoliated malignant cells suggestive of adenocarcinoma. Reduced from  $\times 940$

(Courtesy of Klayman M I *et al* Gastroenterology 29 849 862 November 1955)

ing initial study of the patient. Cytologic studies after partial gastrectomy are not very successful because lavage must be performed with small amounts of solution and satisfactory gastric aspirate is difficult to obtain.

*II Detection of early malignancy* —Klayman and his associates found that the chymotrypsin lavage method of ob-



taining cells aided early diagnosis of gastric carcinoma in three patients

CASE 1—Woman 59, with epigastric pain had benign ulcer crater on the lesser curvature of the stomach seen by x ray and gastrosopy Gastric aspirate disclosed malignant cells suggestive of adenocarcinoma Surgery revealed a healed benign gastric ulcer and sub total gastrectomy was performed A superficial carcinoma of the stomach (in situ?) adjacent to the chronic gastric ulcer was found

CASE 2—Woman 69, had epigastric pain X ray revealed a shallow scar or crater about 2 cm proximal to the pyloric canal and gastroscopy disclosed diffuse atrophic gastritis Cytologic examination revealed malignant cells suggestive of adenocarcinoma (Fig 108) On exploration a small area of induration 2 x 3 mm in diameter was found near the lesser curvature, about 2 cm from the pyloric canal The lesion proved to be carcinoma and subtotal gastric resection was performed

CASE 3—Man 69 had epigastric pain X ray revealed a filling defect in the base of the duodenum and prominent folds of the upper body of the stomach and gastroscopy disclosed prominent gastric folds on the greater curvature Carcinoma cells were found in the aspirate (Fig 109) and subtotal resection was performed A thin 12 mm wide diaphragm like fold of tissue encircling the pyloric rim was in the resected specimen and an adenocarcinoma was noted on the surface of this prolapsing pyloric diaphragm with invasion of lymphatics within the muscularis mucosae

**Cancer of the Stomach** Analysis of 1,152 Cases observed at University of Minnesota Hospitals from 1936 to 1949 is presented by D B Shamon S Horowitz and W D Kelly<sup>8</sup> Histologic or operative evidence of gastric cancer was available in 81% Delay from onset of symptoms to surgical treatment has not been shortened significantly during this period The average age of all patients was 62.8 and a steady increase in older patients was noted Three times as many men as women had gastric cancer

Examination of aspirated gastric contents for free hydrochloric acid and stool examination for occult blood are two important tests that can be performed in the physician's office for early detection of gastric cancer Achlorhydria and/or hypochlorhydria were noted in 87.8% of all patients tested In 83.2% of patients tested for occult blood in the stools guaiac test results were positive

A steady increase in operability and resectability is noted with a resection mortality of 8.8% during 1946-49 (Fig 110) Five year survivals have increased from an overall rate of 37% during 1936-39 to 12.5% during 1946-49 Salvage of 9

additional patients per 100 can be interpreted as a direct result of increased attempts at curative resections. Despite increase of lymph node-positive cases by approximately 20% during the later period, marked improvement in five year survivals enhances the advisability of performing more extensive lymph node dissections. Five year survival rate during the entire 14 years of patients undergoing resection for cure who were subsequently found to have lymph node involvement was 11.4%; of those with negative lymph nodes, 44.1% survived five years or more. During 1946-49, over 70% of patients who had resection for "cure" were lymph node positive, of whom 14.5% survived over five years. Dur-

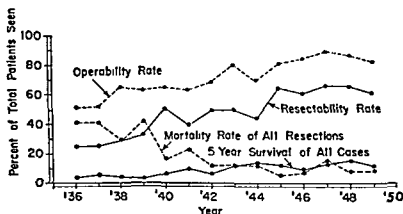


Fig. 110.—Comparison of operability, resectability, mortality and five year survival (Courtesy of Shahon, D. B. *et al.*: *Surgery* 39:204-221, February, 1956.)

ing this same period, 57.1% of patients with negative lymph nodes lived five years after gastric resection.

The role of the surgeon is increasingly important in improving the five year cure of gastric carcinoma. Knowledge gained through "second-look" operations should lead to continuous improvement in five year survivals.

Natural History of Survival in Carcinoma of Stomach, Treated and Untreated is reported by H. M. Pollard and Keith S. Henley<sup>9</sup> (Univ. of Michigan). According to the literature, some patients have survived many years without surgical therapy. Of 531 patients seen at the University Hospital from Jan. 1, 1944 to Dec. 31, 1951, 14 with unequivocal evidence of the disease refused surgery. All 14 had symptoms, and diagnosis was made clinically by x-ray of the stomach, gastroscopy, cytologic study or a combina-

(9) *Gastroenterology* 29 526-535, October, 1955.

tion of the three. The patients had a mean survival time of 144 months, which was broken down to 82 months—the time during which symptoms were present and diagnosis established—and 62 months—from date of diagnosis to death. Mean survival time of 151 patients who had gastric resection was 298 months. Further studies should be made on the natural history of gastric carcinoma in patients without symptoms.

**Gastric Carcinoma Treated with Abdominothoracic Total Gastrectomy.** In 178 cases reported by Bjarne Fretheim<sup>1</sup> (Oslo, Norway), there were 31 (17.4%) postoperative deaths. Eleven were due to infection originating in the operative field, 2 to pneumonia, 2 to lung emboli, 2 to shock, 5 to cardiovascular complications, 2 to incarceration of the jejunal loop in the slit in the diaphragm (enteroanastomosis had not been performed), 2 to intraperitoneal hemorrhage (1 during heparin treatment for thrombosis) and 2 to acute pancreatic necrosis. Three patients died three to four weeks postoperatively from extensive metastases. Most frequent postoperative complications were thromboemboli (10%) and unexplained diarrhea, beginning usually three to four days after operation and lasting a few days to two to three weeks. Other complications included sutural insufficiency and fistula in four (with spontaneous closure in three), subphrenic abscess in six, pleural empyema in two, auricular fibrillation in six, shock in three, unexplained fever in seven and jaundice in four.

One third of the patients with adenocarcinoma died within one year and 27.4% survived more than two years after operation. Over three fourths of patients with muciparous scirrhous died within a year and only 5.5% survived over two years. Three of seven patients with colloid carcinoma died within one year and four survived over two years. Of eight patients with undifferentiated carcinoma, eight with carcinoma simplex and one with carcinoma of undetermined type, none survived two years. Eight of 11 patients who survived over three years had adenocarcinomas and 3 had colloid carcinomas. Correlation with grade (Broders) showed that 75% of the 10% with grade 2 tumors survived over a year and 41% over three years. Of those with grade 3, 46% died within one year and 9% survived over three years.

(1) A M A Arch Surg 71:24-32 July 1955

with grade 4, 75% died within one year and none lived three years. Three-fourths of 29 patients with infiltration into the esophagus died within one year, 3 survived over three years and 1 is living over four years (In this last patient carcinoma was demonstrated in the resection border, and follow-up four years after operation, when he was symptom free, disclosed adenocarcinoma in the anastomosis). Two thirds of patients with extension outside the stomach died within one year, while all 20 patients with no extragastric spread survived more than one year.

Of 63 patients who survived over a year, 44.4% found their symptoms only slightly troublesome and 60% of 52 surviving over two years stated that they were negligible. Operation was regarded as satisfactory by 57% who survived over a year and by 84% who lived over two years (28% have been able to work, at least periodically). Half of those who survived over two years maintained or increased their weight.

Total gastrectomy for gastric carcinoma is recommended in all cases in which the possibility of radical surgery exists when the neoplasm cannot be resected at a minimal distance of 5 cm to both sides of the demonstrated carcinoma. It should not be resorted to for palliation. Combined abdominothoracic incision permits better access and therefore better possibility of radical block dissection than an abdominal or thoracic incision.

Rate of operative mortality and incidence of postoperative complications are so much higher in total than in subtotal gastric resection and postoperative complaints, digestive disturbances, reduced general condition and capacity for work so much greater that subtotal gastrectomy is preferable whenever possible. Patients for whom total gastrectomy was the sole possible form of radical therapy and who have survived for over a year have been sufficiently comfortable to justify the operation.

**Modified Radical Gastrectomy for Cancer of the Stomach** through an abdominal approach with removal of the xiphoid process and of most of the gastric bed in continuity with the stomach and its draining glands, is described by T. Schrire<sup>2</sup> (Cape Town). With this procedure, he proposes to exchange the immediately better results from a slightly

(2) South African M J 29 494-499 May 21 1955

less radical operation for the undoubtedly worse immediate effects and problematic remote improvements from a more extensive procedure

Extension of growth onto the peritoneal surface of the stomach is not entirely hopeless, survival times and five year survivals are about the same as with growths confined to the stomach. Adhesion of growth to adjacent viscera is often due to inflammation preceding the spread of carcinoma, and in many cases the primary growth can be peeled off the liver or transverse mesocolon through this inflammatory zone. When such separation is not possible, resection of the left lobe of the liver, of the transverse colon and of the transverse mesocolon can be performed without much added difficulty. Results have been strikingly improved when a radical local excision has to be made, owing to invasion of adjacent organs and patients are as comfortable when the abdominal wall or viscera adjacent to the stomach have been simultaneously removed.

A large quantity of ascitic fluid, diffuse secondary metastases of the liver and peritoneum or adhesions of the primary growth to the aorta or vena cava are contraindications to any but purely palliative surgery. Irremovable involved glands, or a few secondaries in the pelvis or liver, do not justify hopelessness. Adequate removal of the primary growth occasionally results in involved glands being controlled by some natural process as yet not understood. Hope for such an occasional cure or natural arrest encourages continuance of radical removals in borderline cases.

Local extension of primary growth to the root of the mesentery and around the superior mesenteric vessels is a major difficulty. Sometimes the vessels may be felt pulsating in secondary masses of glands and the latter can then be subdivided and transected and the primary growth freed. It has rarely been necessary to abandon the radical procedure because carcinoma has been cut across, once the vessels have been identified. While cutting carcinoma tissue is contrary to accepted practice palliation has not been any the less effective.

The postoperative course of this operation is little different from that of an ordinary ulcer gastrectomy. Patients often develop a positive gastric balance within 36 hours and

are out of bed on the third day Thoracic complications are, of course, avoided

**Carcinoma of Stomach Autopsy Findings in Untreated Cases** Robert C Horn, Jr.<sup>3</sup> (Univ of Pennsylvania Hosp) reports on autopsies in 74 patients with gastric carcinoma, of whom only 17 had had gastric resection The percentage of theoretically operable but untreated tumors was 17.6% (10 cases) In these 10 cases, exploratory laparotomy was undertaken in 3 and the tumors considered unresectable The disease was limited to the stomach in three, to the stomach and gastric lymph nodes in four and to the stomach, gastric nodes and adjacent viscera in three There was distant spread in 47 One patient was considered inoperable on clinical grounds Three patients died of cardiac disease or pulmonary embolus while awaiting surgery One patient died of a liver abscess six weeks after operation for perforation of the carcinoma, believed to be a benign ulcer until autopsy The remaining two carcinomas were found incidentally in patients with cirrhosis of the liver and extensive prostatic cancer, neither was symptomatic In 16 cases the diagnosis of carcinoma of the stomach was made only at autopsy Of 14 patients with no symptoms of gastric carcinoma, 12 had distant metastases There is thus no valid evidence that a significant number of gastric cancers are coming to autopsy in a state presenting a good opportunity for surgical care Gastric cancer may cause no local symptoms even when it has metastasized widely

Of the 17 patients who underwent gastric resection, 9 had survived for 5 weeks to 27 months All had widespread metastases at autopsy, six without local disease In two, the known residual tumor simply continued to grow postoperatively and in only one was there a genuine local recurrence in the gastric remnant Among the eight patients who died in the postoperative period, four had residual tumor, all with distant spread The likelihood that dissemination usually occurs early in the disease and not from local recurrences is strengthened by the observation that in 266 cases explored surgically, distant metastasis, with or without local spread outside the stomach, was found in 89 on exploration

More extensive surgical procedures than conventional

subtotal gastric resection may well be applicable in selected cases and might bring about a reduction in local recurrences, but they have not effected a reduction in mortality and cannot be expected to unless visceral dissemination takes place from locally recurrent tumor, an assumption that does not seem reasonable

**Gastric Tumors Other than Carcinoma.** Report of Unusual Cases. Samuel F Marshall<sup>4</sup> reports that of 1,700 gastric tumors removed at the Lahey Clinic, 1,567 (92.2%) were carcinomas, 51 (3%) were sarcomas and 82 (4.8%) were benign tumors, including polyps, lipomas, hemangiomas and leiomyomas

Of 51 sarcomas, 35 arose from lymphoid tissue, malignant lymphoma constitutes 70% of gastric sarcomas. There were 16 leiomyosarcomas, no fibro- or angiosarcomas. Symptoms and roentgenologic findings of sarcoma are similar to those of gastric carcinoma, except those of smooth muscle origin, in which x-ray may be characteristic. Leiomyosarcomas tend to bleed and thus cause secondary anemia, but often cause surprisingly little gastric distress. Many sarcomas are resectable and prognosis after resection is much more favorable than for carcinoma. Of 41 patients with sarcoma, 44% lived five years or longer, whereas five year survival following resection for carcinoma was 27.3%. Lymphomas respond to deep x-ray therapy, which should be used four to six weeks after resection. X ray therapy has no effect on leiomyosarcoma, but may be effective in lymphoid tumor too extensive for resection. One patient with extensive Hodgkin's tumor of the stomach lived seven years after exploration and biopsy only. He received intermittent deep x ray therapy and was able to work with little gastrointestinal discomfort until just before death. Leiomyosarcomas are usually slow growing, not prone to metastasis or recurrence. Only four in this series showed leiomyosarcoma metastatic to lymph nodes, liver or lungs. One patient was alive and well 16 years after total gastrectomy and another who had local excision of a large leiomyosarcoma was living 14 years after operation. Nevertheless these are potentially dangerous tumors and should be resected as thoroughly as any carcinoma.

The commonest form of benign tumor is the leiomyoma

which arises from the smooth muscle element of the gastric wall; 28 resections were done for this type of tumor. Benign polyps constituted 1.8% of the 1,700 patients whose gastric tumors were treated surgically; 31 had single discrete benign polyps. Because of the possibility of malignant degeneration, all gastric polyps should be excised, and if carcinoma is demonstrated on frozen section, gastric resection should be done. Benign polyps are usually symptomless unless ulcerated and accompanied by bleeding, which

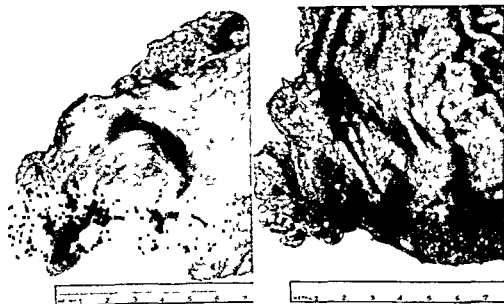


Fig 111 (left) —Resected tumor formed by aberrant pancreas at pylorus

Fig 112 (right) —Opened specimen, mucosal surface of stomach shows extension of tumor mass under mucosa with duct orifice in center

(Courtesy of Marshall, S F S Clin North America 35 693 702, June, 1955)

causes secondary anemia. Achlorhydria may be present. If the polyp originates in the antrum and is pedunculated, occasionally it will prolapse to produce pyloric obstruction. Multiple polyps may be inflammatory or neoplastic. Six patients with multiple polyposis had adenomatous lesions. Most polyps are located in the lower half of the stomach, but in two cases, almost the entire stomach wall was involved. Secondary anemia and achlorhydria are constant in multiple polyposis, and these polyps tend to become malignant; a focus of carcinoma was noted in four cases. Resection should be carried out as for carcinoma.

Lipomas and fibromas of the stomach are extremely rare but may arise in any part of the gastric wall, develop



on the submucosal layer. They may protrude into the gastric lumen or extend toward the serosa. The pathologic nature of this tumor can be determined only by laparotomy and biopsy. Besides the diagnostic need, operation is often necessary because the mucosa over many benign tumors may become ulcerated, causing hemorrhage and secondary anemia.

Aberrant pancreas arising in the stomach was noted in 12 patients. These tumors produce filling defects in the stomach wall (Figs 111 and 112) which may be confused with gastric polyps, peptic ulcer and even gastric carcinoma. If the pathologic condition is recognized at operation, local excision with immediate frozen section for confirmation is sufficient. Many of these tumors are located in the pylorus or first part of the duodenum and are asymptomatic; they are usually discovered incidentally by x-ray examination. If gastrointestinal symptoms are present, they will suggest peptic ulcer, pyloric obstruction, gallbladder disease or functional digestive disorder. Gastric operation is indicated in most instances to rule out malignant tumor or prepyloric ulcer which carries the possibility of malignant degeneration.

**Primary Malignant Neoplasms of Duodenum, Excluding Papilla of Vater.** Clinicopathologic Study of 31 Cases, found in a review of autopsy records for 1910-53, is presented by Arthur Burgerman, Archie H. Baggenstoss and James C. Cain<sup>5</sup> (Mayo Clinic and Found.). The patients included 23 men and 8 women, with an average age of 58.4 years. All the tumors were verified microscopically. There were 27 adenocarcinomas, 2 leiomyosarcomas, 1 lymphosarcoma and 1 reticulum cell sarcoma. Most tumors were in the first and second portions of the duodenum. The majority were either ulcerating or polypoid in type. Average size was 4.6 cm. Grade 3 lesions predominated (37%) among the 27 adenocarcinomas. Five lesions appeared grossly as small polypoid carcinomas. Two lesions, both in the first portion of the duodenum, grossly resembled duodenal ulcers. Both leiomyosarcomas were located in the second portion. Metastases were recorded in 20 cases. The sites most frequently involved were the regional lymph nodes and the liver. In only two cases were there metastatic lesions outside the ab-

domen, in one to the mediastinal lymph nodes and in the other to the lung and mediastinal lymph nodes

Abdominal pain was recorded in 23 cases, usually for two to six months, and loss of weight in 23, usually for three months to one year Vomiting was present in 17 cases, hematemesis in 4, melena in 9 and jaundice in 7 There was a paucity of physical findings An abdominal mass was found in six cases Anemia was present in 17 There was no correlation between the type or location of the lesion and the amount of gastric acids

X-rays were made in 22 cases, and a lesion of the duodenum was thought to be present in 15 A malignant neoplasm was diagnosed in 11 and a duodenal ulcer in 4 A correct antemortem diagnosis was made in nine cases, all by x-ray

**Afferent Loop Syndrome.** About 85-90% of patients treated for gastroduodenal ulcer by subtotal gastrectomy are improved Formerly, all who showed new symptoms postoperatively were said to have the dumping or post-gastrectomy syndrome, but recently it has been shown that symptoms may arise from multiple causes and that proper management depends on accurate evaluation of the underlying pathophysiology The afferent loop syndrome has received considerable comment in the English literature but still is not recognized by many American surgeons

The condition develops only after the Billroth II gastrectomy as symptoms are due to partial or recurrent obstruction of the afferent loop, prohibiting passage of bile and pancreatic juices from the duodenum into the efferent loop Obstruction may be due to adhesions, to weight of a distended colon, to internal herniation or to volvulus It is most likely to occur following the Finsterer Lake type antecolic right-to-left anastomosis associated with a Hoffmeister valve, when the afferent loop is long or when a very high resection has been performed The syndrome causes chronic recurring symptoms rather than one acute episode, and the vomitus contains bile because vomiting usually occurs when the contents of the afferent loop are emptied

The patient usually has nausea 10-20 minutes after eating which persists for a few minutes to an hour Vomiting, which may occur after each meal or only occasionally, gives immediate relief, and symptoms do not recur until more

food is ingested. The vomitus usually consists of bile stained fluid unmixed with food, in volumes of 500-1,000 ml. If vomiting is severe, food is finally ejected as the disturbed motility spreads down the gastrointestinal tract, but bilious regurgitation always precedes appearance of food particles. Symptoms are most severe after a fatty meal resulting in maximal liberation of bile.

X-rays may show little or no filling of the afferent loop after ingestion of small amounts of barium, but this segment is almost invariably outlined, without special maneuvers, if the patient ingests barium until he feels uncomfortably full. When x-ray findings are definite, little doubt of diagnosis exists, but studies may be performed when obstruction is minimal so that diagnosis may be missed.

In an effort to gain additional objective evidence, George L. Jordan, Jr.<sup>6</sup> (Baylor Univ.) devised the following test.

**TECHNIC**—A mercury weighted, large lumen Levine tube is passed into the efferent loop 6-12 in beyond the gastrojejunostomy stomal, under roentgenographic control. A fasting specimen is aspirated and the patient is fed a liquid meal of 60 ml. ediol,<sup>\*</sup> 240 ml. milk and 180 ml. of 40% glucose solution. Aspiration of jejunal content is made at 1 minute and then at 5 minute intervals until good mixing of bile with the ingested meal is seen. A positive test result indicating afferent loop obstruction is recorded when bile is absent from the jejunum during the period of symptoms and its appearance coincides with disappearance of symptoms.

Relief can be obtained by any surgical procedure that eliminates the site of obstruction. In Jordan's two patients, enteroenterostomy produced satisfactory results.

**Surgical Management of Postanastomotic and Postgastrectomy Malfunctions** According to M. E. Steinberg<sup>7</sup> (Univ. of Oregon), the side effects following gastric operations become more understandable when interpreted on the basis of the following separate mechanisms: (1) gastric pouch malfunction; (2) dumping malfunction (efferent loop syndrome); (3) reflux malfunction with afferent or efferent loop stasis. He describes 33 patients who had had 68 miscellaneous operations and who later had 39 corrective operations for various disabling postanastomotic and postgastrectomy malfunctions. The average weight loss in 24 of these patients before corrective surgery was 30 lb. The corrective surgery gave significant or satisfactory results in

(6) Surgery 38:1027-1035, December, 1935.

(7) A.M.A. Arch. Surg. 71:95-108, July, 1935.

25, who were able to return to work. The average gain in 19 patients was 22 lb. In five, the results were inconclusive, and in two the operation was a failure.

Crippling side effects because of various mechanisms of reflux and enteric loop stasis were more frequent than crippling from dumping. Postanastomotic reflux malfunction, with and without afferent or efferent loop stasis, can be recognized and rectified by definitive surgical methods. An enteroenteroanastomosis does not regularly prevent reflux. The original gastrojejunojunoplasty was introduced by Steinberg and Starr in 1934. Since 1946, an improved method of gastrojejunojunal anastomosis, the "pantaloon" method [Steinberg, 1949 YEAR BOOK, p 408], has been used in 330 patients for benign and malignant lesions and for postoperative malfunctions, with an over all mortality of 15%, as compared with a mortality of 17% in 591 patients with gastrectomy by conventional methods of anastomosis for all benign lesions. The end results in patients with conventional anastomoses and in those with the pantaloon anastomosis when used as the initial operation were equally satisfactory.

Undesirable side effects after the Hofmeister retrocolic anastomosis frequently result because of deviation from the technic standardized by Finsterer and also because of injudicious removal of increasingly larger parts of gastric tissue, dictated by faulty interpretation of the results of animal experimentation. The pantaloon anastomosis has obvious technical and functional advantages over the conventional method in all primary operations when all or most of the stomach is sacrificed and has proved of singular merit in relieving crippling postanastomotic side effects.

The success of the pantaloon anastomosis will depend on added time and diligence commensurate with an enlarged technic. Unless the surgeon is experienced in gastric surgery he should approach this procedure with restraint.

► [There seems to be some disagreement between Steinberg and the author of the preceding article, Jordan, as to whether the dumping syndrome should be ascribed to difficulty in the efferent or the afferent loop.—Ed.]

**Tuberculosis Occurring after Gastrectomy** was investigated by Karl Boman<sup>8</sup> (Karlshamn, Sweden) in 906 patients in four different sanatoriums. In 43 with peptic ulcer,

tuberculosis followed the ulcer in 32, in 23 with gastrectomy the tuberculosis followed operation in 20. Most patients were males.

Of 395 patients who underwent the Billroth I or II operation for ulcer, 16 had had tuberculosis before surgery and none had recurrence afterward. Tuberculosis, usually a mild form, was diagnosed after the operation in 18 (an average of 10.4 years postoperatively). Of 93 patients who had died, 16 died of pulmonary tuberculosis, in contrast with an expected incidence of 6. The deaths occurred on the average of 7.5 years postoperatively.

The study demonstrates that the number of deaths from tuberculosis is statistically excessive among persons who have undergone gastrectomy for gastric ulcer, it also appears probable that the incidence of tuberculosis is higher in that category than among subjects with normal gastric function. Gastrectomy is a more important factor in predisposing to tuberculosis than ulceration as such. Tuberculosis followed equally often after the Billroth I and II operations, but the course of the disease was more frequently virulent and the death rate higher after the Billroth II operation (not verified statistically). The period immediately after the operation appears to be the most critical.

---

## THE SMALL INTESTINE

**Noble Plication Operation for Chronic Recurring Intestinal Obstruction** is recommended by James Barron and Laurence S. Fallis<sup>9</sup> (Henry Ford Hosp.) for patients with adhesions. The operation should be carried out as a planned procedure after careful preparation of the patient, with special emphasis on nutritional deficiency.

**TECHNIC**—Through a transverse abdominal incision just above the umbilicus the omentum and entire jejunum and ileum are freed by sharp dissection. Occasionally segments of the small bowel have to be resected. The plication is started at the lower ileum or the upper jejunum after complete freeing of the structures. Interrupted fine silk sutures on small French needles or straight intestinal needles are used to unite the mesenteric attachment of the intestinal loops. The blood supply should not be damaged. Three key sutures are used

at the start of each loop plication (Fig. 113), the first placed near the base of the mesentery and the second and third in the mesentery near the bowel wall at each end of about 8 in. intestinal loops. This produces a triangular-shaped area, with the apex represented by the suture at the base of the mesentery. The mesentery then is approximated with interrupted sutures between the three key points. The same procedure is performed on the opposite side of the mesentery, the plication being repeated on alternate sides until the entire jeju-



Fig. 113—Placement of three key sutures. (Courtesy of Barron, J., and Fallis, I. S.: *A.M.A. Arch. Surg.* 71 518-522, October, 1955.)

num and ileum are plicated (Fig. 114). At completion of the operation, the omentum, when present, is placed between incision site and plicated small intestine.

The operation was performed in 40 patients. A complete plication of the entire jejunum and ileum was carried out in 17. None of these had fewer than three previous abdominal operations, and seven were taking varying amounts of narcotics for pain. Duodenal ileus was present in four, all of whom were asthenic. None of the patients had subsequent attacks of intestinal obstruction during a follow-up of six

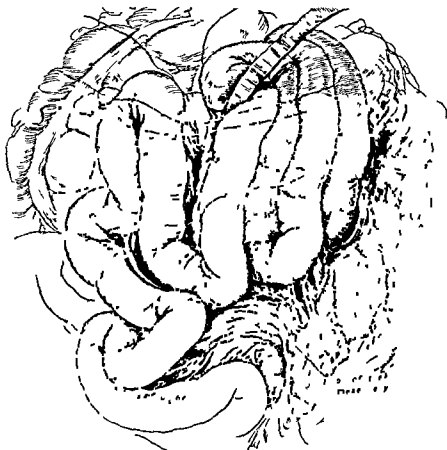


Fig 114—Plicated loops of bowel 78 in long including entire jejunum and ileum. Plication is carried out on alternate sides of mesentery (Courtesy of Barron J and Fallis L S. A M A Arch Surg 71:518-522, October 1955.)

months to more than five years. Most had shown a satisfactory weight gain, and none were taking narcotics.

► [Certainly nobody could ask for better results—Ed.]

**Noble Plication Procedure.** Application to Acute and Chronic Recurrent Small Bowel Obstruction due to chronic adhesive peritonitis with visceral or parietal peritoneal damage is reported by Gordon K. Smith<sup>1</sup> (Univ. of Southern California). Plication was performed with a continuous interval-locked chromic gut suture placed midway between the mesenteric and antimesenteric borders (Fig 115). In partial plication, leaves of mesentery were closed to prevent herniation of small bowel through these potential foramina. Where damage to peritoneum was restricted to a short bowel segment, partial plication was deemed adequate. Where 'skip' areas of normal bowel intervened or there

(1) A M A Arch Surg 70:801-807, June 1955.

was extensive loss of visceral peritoneum, complete plication was done

Twelve patients with acute small bowel obstruction who had total Noble plications were well and asymptomatic Two of three with chronic obstruction had additional surgery One had revision of the plication because of separation of the loops, causing partial obstruction The other patient had strangulating obstruction of the upper jejunum six months after total plication The only other serious compli-

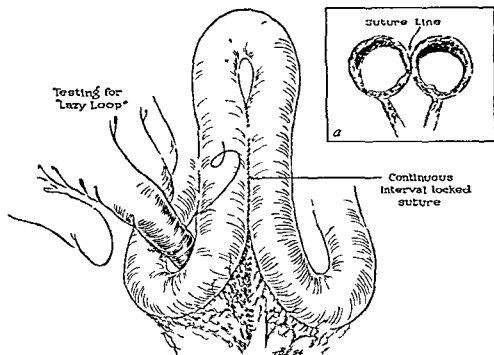


Fig 115 —Principles of technique of Noble plication. Continuous interval locked chromic suture approximates bowel and mesentery leaving lazy loop. Inset shows approximate site of suture in bowel wall (Courtesy of Smith G K. A M A Arch Surg 70 801 807 June 1955)

cation was a pelvic abscess in a patient who had small bowel resection and total plication

Of 13 patients with partial plication, 3 required further surgery One, in addition to partial plication, had a free omental graft over a raw area on the sigmoid and secondary strangulating obstruction developed where the graft had become absorbed Another patient, asymptomatic for two years after partial plication, had simple obstruction requiring laparotomy Following enterolysis, peritoneal damage was so severe that total plication was performed Death of a third patient was attributed largely to delay of 72 hours after onset of symptoms before surgery was performed



Postoperative distention was variable and sometimes troublesome. In some cases return of peristalsis was delayed 8-10 days and x-rays showed persistence of small-bowel gas up to 6 weeks after plication.

The operation was apparently more successful in acute obstruction, suggesting that low grade peritonitis aided in agglutination of loops of small bowel. Plication of the small bowel is not without hazard. Possible morbidity contraindicates its use as a prophylactic procedure except in carefully selected cases.

**Prevention of Recurrent Small Bowel Obstruction Due to Adhesions.** The technic described by Raleigh R. White<sup>2</sup> (Temple, Tex.) is based on the concept that splinting of large, more or less symmetrical loops of bowel results in controlled adhesions and prevents sharp angulation or kinks causing subsequent obstruction (Figs. 116 and 117).

**TECHNIC.**—Preoperatively, if possible, a long intestinal tube (Mil-



FIG 116.—Technic of passing long intestinal tube down into distal bowel with vein stripper (Courtesy of White, R R Ann Surg 143 714 719, May, 1956)

ler Abbott or Cantor type) is passed into the small bowel down to the point of obstruction. After the abdomen is opened, the intestine is deflated and the contents are removed by the Barnes aseptic long trocar technic. All adhesive bands are divided and bowel links are released, with resection of a deformed or scarred segment if necessary. The distal tip of the long intestinal tube is then located and a small opening made in the intestine at this point, sufficient length of tube to splint the entire gut is pulled down. With the Meyer vein stripper as a guide the tube is threaded down to but not through the ileocecal valve requiring one and occasionally two additional small incisions in the bowel (Fig 116). Bowel openings are closed transversely with fine chromic and interrupted fine silk sutures. Care is taken to prevent contamination by bowel contents. In some instances, the in-

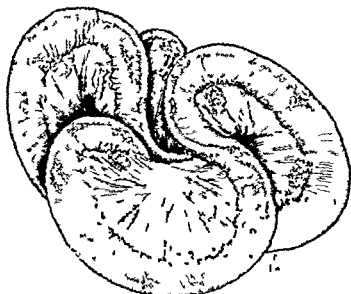


Fig 117—Large coils of denuded bowel maintained in position by splinting on long intestinal tube until controlled adhesions can form (Courtesy of White R R. *Ann Surg* 143 714 719 May 1956)

flated bag of the long intestinal tube can be "milked" down into the lower bowel without enterotomy but usually not without undue trauma.

When a long tube cannot be passed preoperatively, an enterotomy is made above the most proximal arc of denuded bowel and splinting carried out caudally. The distal tip of the tube is brought out of the cecum as a cecostomy to permit later removal. This procedure may afford more comfort to the patient postoperatively than insertion of the tube nasally. When introduced through the nose virtually the total length of the long intestinal tube is required to place the tip comfortably in the terminal ileum.

Antibiotics are administered postoperatively and the tube is left in place about 10 days. A Levin tube is useful to decompress the upper gastrointestinal tract during the first 48 hours. The patient receives a low residue diet and early ambulation is encouraged. Mineral oil is given by mouth. Extraction of the tube is facilitated if the balloon is removed at operation.

This splinting procedure has been used on 16 selected patients, and 12 of 14 followed for one to six years have obtained satisfactory results

**Strangulation Obstruction: Antibiotic Protection in dogs,** using a nontoxic route of administration, is described by Isidore Cohn, Jr.<sup>3</sup> (Louisiana State Univ.)

**METHOD**—Operations, using aseptic techniques, were performed under intravenous nembutal<sup>®</sup> anesthesia (Fig 118) The bowel was di-

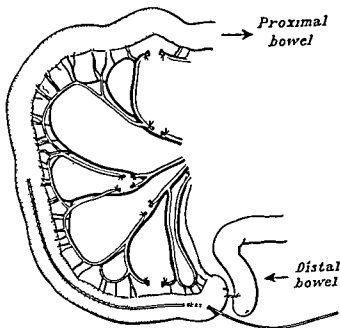


Fig 118—Operative procedure showing division of bowel closure of two ends and approximation of distal and proximal bowel by single suture (Courtesy of Cohn<sup>1</sup> Jr. Surgery 39 630 641, April 1956)

vided 75% of the distance from ligament of Treitz to cecum and the two ends were closed with Parker-Kerr sutures, after cultures were taken from the lumen. Chlortetracycline (750 mg in capsule) was placed in the portion to be strangulated. The two segments of bowel were approximated to prevent intussusception of distal segment. A plastic tube, inserted in normal bowel, was threaded into the portion to be strangulated and the other end exteriorized for postoperative administration of antibiotics. A 30 cm segment of proximal bowel (stippled) was strangulated by isolating, dividing and ligating all its veins. Vessels parallel to the bowel at each end of the segment were divided and ligated. Latex tubes were placed in the peritoneal cavity for postoperative collection of fluid.

Chlortetracycline dissolved in 10-15 ml sterile saline was injected into the strangulated segment through the plastic tube. 250 mg every

(3) Surgery 39 630 641 April 1956

4 hours for first 48 hours, then every 8 hours until reoperation. Penicillin was given twice daily intramuscularly in doses of 300,000 units.

Five dogs subjected to this experiment survived to be reoperated on 118-142 hours after strangulation. At reoperation the strangulated segment was resected and intestinal continuity restored in three animals, which survived three to nine months. Two were killed for immediate pathologic study.

After strangulation, animals walked about and seemed in good condition. Weight loss became more severe with time, as intravenous alimentation had to be supplied in relatively small fluid volume. Vomiting ranged from two to nine episodes. Hematemesis, which occurred in only two dogs, appeared before recovery from anesthesia in both.

Clostridia was not found in cultures from bowel lumen at the first operation. Two cultures of peritoneal fluid showed hemolytic *Escherichia coli* in one and no organisms in the other. White cell counts of blood rose to a peak in first 24-48 hours, declined slightly and then rose slightly before reoperation. White cell count of peritoneal fluid rose steadily. Adequacy of fluid therapy was demonstrated by satisfactory output and relatively constant values for hemoglobin and hematocrit. Total blood requirements were reduced from 660-1,085 ml in nonantibiotic series to 200-875 ml. In ml/kg/24 hours, values in the present series were 2.98-11.1, contrasted with 24-72 in animals not treated with antibiotics. Electrolyte administration was approximately one fourth that in the nonantibiotic series. Maximal peritoneal fluid output, 229 ml, was only about one-third the minimal output, 603 ml in nonantibiotic series. Urine and vomitus were about 40% of average values.

The strangulated segment of bowel appeared essentially normal at reoperation, except that it was thicker and shorter from contraction of the muscular wall and hemorrhage and edema following strangulation. The mucosa was indistinguishable from the normal. Normal gross appearance of strangulated segment was confirmed by microscopic study.

Survival in dogs with strangulation obstruction, achieved by use of antibiotics, emphasizes the importance of the bacterial phase of toxicity in strangulation obstruction.

► [This is a cleancut experimental study with striking results that should be immediately applicable to the human.—Ed.]

**Postoperative Pseudomembranous Enterocolitis Due to Staphylococcus** is an increasingly frequent serious complication for which, as George B Sanders and David W Kin naird<sup>4</sup> (Univ of Louisville) emphasize ill advised use of antibiotics may set the stage Defloration by antibiotics of the normal intestinal content is a prerequisite to enterocolitis or aids its development Probably the high carrier rate of resistant staphylococci from widespread use of penicillin and other antibiotics is an important factor In its severest form, enterocolitis is probably due largely to luxuriant overgrowth in the intestine of resistant strains of *Micrococcus pyogenes* var *Staphylococcus aureus*, which produce a potent enterotoxin One institution reported 60% penicillin resistant and 41% streptomycin-resistant strains of this organism in 1948 with none resistant to chlortetracycline and oxytetracycline, whereas by late 1953, 92% of resistant strains were found

A patient who receives antibiotics in preparation for a major abdominal or gastrointestinal operation becomes extremely vulnerable to resistant staphylococci thriving in the hospital The patient himself may be a carrier, and a large percentage of hospital personnel are carriers These ubiquitous organisms can sweep down from the upper digestive tract into the intestine shortly after stressful surgery, overgrow with astounding rapidity, develop a potent enterotoxin and create severe, possibly fatal, enterocolitis

Copious diarrhea is the commonest symptom of pseudomembranous enterocolitis, and this with vomiting and drainage from gastrointestinal suction apparatus or from *ileostomy or colostomy stomas may result in overwhelming fluid and electrolyte loss Thirst, abdominal distention, fever, restlessness and confusion are common, and fatigue, exhaustion and shock at times appear with astonishing rapidity Earliest reported fatal cases were described as postoperative shocklike states The characteristic pathologic findings are ulceration focal infection and sloughing of mucous and submucous coats, predominantly of the small bowel, with abundant overgrowth of staphylococci*

In addition to refraining from indiscriminate use of penicillin and other antibiotics in trivial infections or in situations where specific indications for particular antibiotics

are lacking, curtailment of the prophylactic use of antibiotics in clean surgical cases is wise and desirable. A return to scrupulous observation of traditional principles of masking, hand washing and wearing of gloves by personnel attendant on surgical patients in the wards is recommended.

Complete withdrawal of all antibiotics should be made as soon as diagnosis of enterocolitis is made. Fluids lost should be measured and adequate fluid and electrolyte replacement carried out, along with measures to counteract shock. The drug to be relied on at present appears to be erythromycin orally, if possible, 200-300 mg every four hours. Effective prompt treatment usually results in alleviation of symptoms in 24-48 hours.

**Brunner-Type Glands in Regional Enteritis** C A Kawel, Jr, and Henry Tesluk<sup>5</sup> (Henry Ford Hosp) examined varying lengths of ileum resected from 34 patients with regional enteritis. The morphology of the aberrant glands could be recognized by routine staining but were further differentiated by indulin-mucicarmine stains. Brunner gland cells stain red with mucicarmine and intestinal mucous secretions stain black with indulin.

In the ileum of 16 patients, Brunner-type glands were found (Fig 119). The glands resembled the Brunner glands in the duodenum and pylorus of the stomach. They begin abruptly, and no transitions with intestinal glands are seen. Changes of this type were not encountered in bowel resected in other inflammatory diseases, except in one case of tuberculous enteritis.

No relation could be established between microscopic findings, age of patient, duration of symptoms, severity of illness or length of bowel involved or resected. However, all 16 patients had been operated on previously because of their disease, and in two thirds symptoms recurred. None of the 18 patients without Brunner-type glands have had recurrences.

Possible explanations for the development or occurrence of these peculiar glands must include both heterotopia and metaplasia. Indulin stain studies indicate that the secretion of these glands is chemically different from that of the intestinal mucosa. This change is not merely morphologic but represents a change in function.

(5) *Gastroenterology* 28:910-920, May, 1955.



Fig 119—Mucosa of ileum showing large numbers of Brunner-type glands in case of regional enteritis. Hematoxylin-eosin; reduced from  $\times 70$  (Courtesy of Kawel, C A, Jr., and Tesluk, H. *Gastroenterology* 28 810-820, May, 1955.)

There is no evidence that such changes occur before onset of regional enteritis. It is much more likely that they follow its development. The presence of such changes should make later recurrence more probable.

**Treatment of Intestinal Obstruction in the Aged** and causes of death were analyzed by George Wantz and Frank Glenn<sup>6</sup> (New York Hosp.-Cornell Med. Center) in 120 patients over 65 (average age 71.8) seen from 1944 to 1954. Average age of 19 (15.08%) patients who died was 74.8. Chief causes of intestinal obstruction were external hernias in 39 (32.51%), adhesions in 28 (23.3%) and neoplasm in 21 (17.5%). Emergency operation was performed as definitive treatment in 110, with 14 deaths (12.73%). Of 10 nonoperative patients, 5 survived; of the 5 who died, 4 were too ill for surgery, and in 1 diagnosis of intestinal obstruction was not made.

There were 80 instances of small bowel obstruction with 11 deaths (13.7%); simple small bowel obstruction occurred in 45, with 4 deaths (11.2%). Of 35 patients with strangu-

(6) *J. Am. Geriatrics Soc.* 3 974-983, December, 1955.

lated small bowel obstruction, 7 died (20%), 4 of these were not operated on. Of 40 patients with large bowel obstruction, 8 died (20%). Of 35 patients with simple and 5 with strangulated large bowel obstructions, 7 and 1, respectively, died. This high mortality is not surprising because almost half the large bowel obstructions were due to carcinoma and three of the eight deaths were from terminal carcinoma and Long-tube decompression in 11 patients with small bowel obstruction was successful in only 2. It delayed operation in 9, and 1 died of fluid and electrolyte imbalance following operation for lysis of adhesions. The other eight were saved, without complications.

Shock and peritonitis were the commonest causes of death. In eight, they were directly due to effects of intestinal obstruction, in two, as complications of the operation. One died of fluid and electrolyte imbalance. Four deaths were cardiovascular, and four were due to carcinomatosis.

The study indicates that age and concomitant diseases are secondary as causes of death and that early application of reliable established therapeutic procedures reduces mortality. Maximal benefits from such preoperative preparation as decompression, restoration of fluids and electrolytes and antibiotics for control of infection are desirable, but unnecessary delay in hope of better preparation is hazardous. Early treatment is the safer way to avoid catastrophic effect of late mechanical intestinal obstruction. For a successful outcome, all phases of operation must be accurately and swiftly performed. Choice of operation depends on nature of the obstruction and condition of the patient. Best results are obtained if the procedure is short and simple, with minimal trauma. Formidable resections and correction of incidental pathologic conditions increase morbidity and mortality.

---

### THE APPENDIX

Diminishing Mortality from Appendicitis. Data from Johns Hopkins Hospital presented by James R. Cantrell and Edward S. Stafford<sup>7</sup> (Baltimore) show that the overall mortality from appendicitis depends almost entirely on

(7) *Ann Surg* 141:749-758, June 1955



the incidence of perforation. There have been no deaths from appendicitis without perforation since 1947 and mortality during the past 25 years has been approximately 0.1%, almost reaching the base line level for general anesthesia, i.e., about 0.08%. Mortality from appendical perforation has also steadily declined. Among 85 such cases observed from 1928 to 1931, there were 16 deaths (18.8%). In the 1931-39 series, there were 48 deaths in 479 cases (10%), in 1939-47 series, 23 in 325 (7%) and in the 1947-54 series, 6 among 219 (2.7%). Factors responsible for this improvement include use of fluids and electrolytes, blood transfusions, intestinal decompression, antibiotics and early ambulation.

Striking common features among fatal cases of appendical perforation were prolonged duration of the disease (4.21 days) and presence of generalized peritonitis. There were no deaths in patients with appendical abscess, representing 44% of the perforation group. Failure of the body to localize an infectious process may be attributed to a particularly virulent organism and/or inadequate resistance. These facts cannot be altered, so further reduction of the mortality from appendicitis is primarily dependent on prevention of perforation. This, in turn, depends on improved education among physicians, especially the family doctor or internist who first sees these patients, and laymen.

If perforation is to be eliminated, removal of some normal appendixes must be accepted. 20-25% normal appendixes in patients with a preoperative diagnosis of acute appendicitis should not be regarded as unreasonable, especially since a significant percentage of these will have other acute conditions requiring operation. Every effort should be made to establish an exact diagnosis, but if this is impossible and appendicitis is suspected, exploration is mandatory. It is far better to subject a moderate number of patients to a theoretically unnecessary operation than to let one suffer perforation.

► [Probably the principle danger in acute appendicitis is the taking of cathartics. If the public could be effectively educated about the danger of that practice the mortality would be even lower than the low one quoted by the authors of this article.—Fd.]

**Appendicitis and Ileus.** E. Weisschedel<sup>8</sup> (Univ. of Freiburg, Germany) reports that among 15,000 appendectomies

performed from 1938 to 1945, 269 patients (18%) died. Peritonitis with subsequent paralytic ileus accounted for 59% and mechanical ileus for 11% of the deaths. Adynamic ileus is nearly always caused by bacterial infection of the abdominal cavity. Loss, through vomiting, of large quantities of fluid and vital organic and inorganic constituents leads to increased blood viscosity and consequently to severe impairment of circulation. The intestine becomes excessively distended by gas derived from decomposition of accumulated intestinal contents. Resulting displacement of diaphragm and heart, with compression of the inferior vena cava, causes severe impairment of respiration and circulation. General condition deteriorates due to absorption of toxins from the distended bowel, renal impairment resulting from anhydremia and loss of electrolytes (chloride and potassium).

In treatment of paralytic ileus, peritonitis should be controlled by removing the source of infection and any pus from the abdominal cavity and by antibiotics locally and parenterally. Intestinal paralysis must be counteracted. Suction drainage of gas by long intestinal tubes, replacement of lost fluid, electrolytes and proteins by intravenous drip and stimulation of intestinal muscles by drugs are essential.

Mechanical ileus usually develops some time after onset of appendicitis, when scars and adhesions have caused morphologic changes. Instillation of antibiotics into the abdomen tends to prevent adhesions because infections are counteracted. In all types of mechanical ileus, except that caused by extensive membranous adhesions, operation should be performed early to relieve obstruction, especially in presence of strangulation or invagination. If surgery is done within the first 24 hours, the patient usually recovers.

Modern treatment methods have greatly reduced the mortality following appendectomy. Among 2999 appendectomies performed during the past two years, death rate was 0.17%.

**Appendicitis in the Aged** is discussed by H. Steiner<sup>9</sup> (Vienna) on the basis of results obtained with either surgical or conservative treatment during the same period (1953-54). Of 717 surgical cases, 94 were in patients over 50 (63

(9) Wien klin Wchnschr 68:369-370 May 11 1956

women) Four of six deaths occurred in this age group Of 10 elderly men with perforations, 2 died, 1 with a mesenteric infarct and peritonitis and the other of pulmonary embolism Two deaths also occurred among six women with perforated appendixes, one from diffuse peritonitis and the other from pulmonary embolism Other complications in these aging patients included disturbances of wound healing in 16, thrombosis in 2 (women), 6 had both these complications Thus fatal and nonfatal complications occurred in 35.5% of 31 older men (contrasted to 12.3% in younger males) and in 28.6% of older women (7.4% in young women) In patients with chronic appendicitis in the older age group complications occurred in 25% of the women and in 21.4% of the men

Among 157 patients treated conservatively, 87 were over 50 (69 women) Two women died, but neither death resulted from appendicitis In one with a clinical diagnosis of appendicitis, necropsy showed uremia The other died of cardiac failure In both, operation was contraindicated

In view of the high incidence of complications in older patients after appendectomy, Steiner increasingly has used conservative treatment Appendectomy is done only when perforation is suspected or when there is progression of acute symptoms All conservatively managed patients must be under careful observation and, after acute symptoms subside, must have thorough clinical examination

Study of 50,000 Specimens of Human Vermiform Appendix, representing material gained by co operation of 250 surgeons and 11 hospitals from 1924 to 1955, is reported by Donald C Collins<sup>1</sup> (College of Med Evangelists) The source of 90.67% of the material was surgically removed fresh specimens, the remaining 4,665 appendixes (9.33%) being obtained post mortem Of the 45,335 surgically removed appendixes 25,865 (57.05%) were either diagnosed as "chronic" by the pathologist or prophylactically removed by the surgeon i.e. within the range of normal There were 12,018 instances of acute appendicitis of which 4,911 (10.83%) were either perforated or gangrenous Incidence of "subacute appendicitis" was 13.64% A small group of 633 (1.4%) showed miscellaneous significant pathologic lesions unrelated to inflammation or specific disease

(1) Surg. Gynec. & Obst. 101:437-445 October 1955

Hospital mortality of acute appendicitis decreased from 13.9% in 1925 to 0.01% in 1955. Recent recognition of common incidence of a benign type of juvenile histoplasmosis led to review of earlier microscopic slides that revealed that at least 78.1% presented characteristic *Histoplasma capsulatum* (Darling), usually in the "germinal-centers" of the submucosal lymph nodes. In 33.7% of the patients, specimens were removed during the course of various specific diseases and afforded a valuable means of learning what histologic changes occurred in the vermiform appendix.

In 13.02% of cases (including histoplasmosis), appendices showed presence of mycologic parasitic disease. Parasitic worms were found in 1.91%. Benign tumors were encountered in 4.34% of these appendices. Primary malignant tumors were present in 632 (1.26%). Unusual foreign bodies were found within the lumens of 1.28% of specimens. Only 224 instances (0.45%) of appendical fistula were recorded. Among interesting miscellaneous rarities were 4 examples of proved congenital agenesis, 2 of true congenital duplication, 2 of intussusception and 15 with situs transversus viscerum abdominis (10 of these had dextracardia).

Of 6710 appendices, 9.54% showed total lumen obliteration, 25.52% varying degrees of incomplete lumen obliteration and 64.92% completely patent lumens. According to 33810 descriptions of position occupied by the appendix within the abdominal cavity, 74% of the appendices were anterior to the cecum and 26% were retrocecal.

**The Tissue Committee** V **The Normal Appendix** W. E. Lawton, John E. Lutz and Bert Bradford, Jr.<sup>2</sup> (Charleston) investigated the part played by the tissue committee in reducing unwarranted appendectomies in a 240 bed, open staff general hospital with 26 participating general surgeons. The criterion of diagnosis of acute appendicitis was leukocytic infiltration of the wall. In 249 consecutive appendectomies, 1952-55, preoperative diagnosis of acute appendicitis was made in 226. Diagnostic error in 1952 was 24.1%, in 1953, 23.7% and in 1954, 13.3%. This reduction is believed a direct result of activities of the tissue committee. Removal of an occasional normal appendix may be justifiable but removal of as high as 50% of normal appendices, as practiced by some surgeons, cannot be condoned.

(<sup>2</sup>) West Virginia M. J. 51:345-348 November 1955

Appendectomies, with preoperative diagnosis of acute appendicitis, represented only 4.26% of all major operations in 1954. In 35 cases with rupture, the rupture apparently was present at hospitalization in 31, with no significant differences noted in yearly rate of rupture. Of four cases in which rupture possibly occurred after hospitalization, one was observed two days by the medical service without surgical consultation, and another involved a woman eight months pregnant, with atypical signs and symptoms. Of 42 cases (32 women) in which diagnosis of acute appendicitis was incorrect, other disease was found in 28. Surgery was justified in approximately 78% of these cases.

Interval appendectomy for chronic or recurrent appendicitis was done in 23 cases—8 in 1952, 11 in 1953 and 4 in 1954. Generally speaking, operation for chronic appendicitis, except in rare instances, is not approved by the tissue committee.

A completely honest pathologist is essential to proper functioning of a tissue committee, which the authors believe can be an asset to any hospital, to provide maximal protection for both patient and surgeon.

► [It is encouraging to read some words of praise for the tissue committee. When properly organized and with good support from the staff there can be no doubt at all about the effectiveness of such a committee.—Ed.]

---

## THE COLON AND RECTUM

**Hemorrhoids and Their Surgical Treatment.** A Description of the St. Mark's Hospital Operation for Hemorrhoids is presented by C. Naunton Morgan<sup>3</sup> (London). A hemorrhoid is a vascular swelling formed in either the internal or the external venous hemorrhoidal plexus, or both. The internal plexus is situated in the submucous space above the valvular line and is covered by columnar mucous membrane. The external plexus lies under the true skin of the anal verge in the subcutaneous perianal space. The two plexuses communicate with each other. There is an interhemorrhoidal depression between the two plexuses. Enlargement of the internal hemorrhoidal plexus with an associated increase of connective tissue results in the formation of an internal

hemorrhoid; while a swelling due to distention, thrombosis or rupture of veins in the external hemorrhoidal plexus, or a consequent hypertrophied skin tag, forms an external

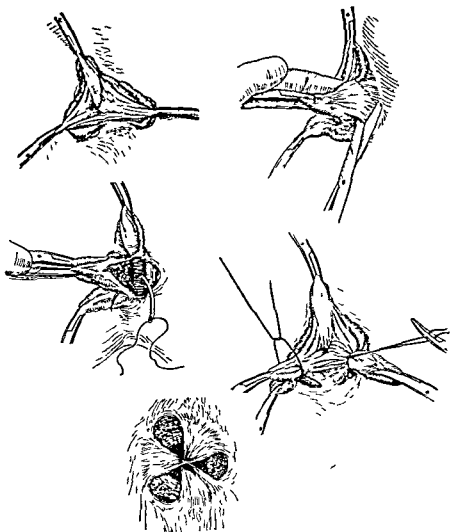


Fig 120 (top left) —Triangle of exposure

Fig 121 (top right) —Hemorrhoidectomy, commencement of dissection

Fig 122 (center left) —Dissection completed, lower end of internal sphincter and longitudinally placed fibers passing to dissected hemorrhoid exposed

Fig 123 (center right) —Left lateral hemorrhoid has been ligated, right posterior hemorrhoid in process of being ligated

Fig 124 (bottom) —Three flat perianal wounds with complete skin bridges in between

(Courtesy of Morgan, C N S Clin North America 35 1457 1464, October, 1955)

hemorrhoid. A combination of internal-external hemorrhoid may be formed.

Internal hemorrhoids do not cause pain unless there is thrombosis, infection or a fissure. Bleeding at stool and vague discomfort are the main symptoms. Prolapse of internal hemorrhoids is a chronic process associated with

laxity of the anal musculature Hemorrhoids at first are reduced spontaneously after defecation but later require digital reposition External hemorrhoids are painful and tender Hypertrophy of the perianal skin folds, forming skin tags, may occur after prolonged chronic infection or thrombosis Diagnosis is made by inspection, digital examination and proctoscopy Sigmoidoscopy is necessary in all cases

Surgery is the only sure cure for prolapsing hemorrhoids The St Mark's technic for internal hemorrhoids follows

**TECHNIC**—With the patient in the lithotomy position the perianal skin tags of each of the three primary hemorrhoids is grasped with a pair of nontoothed dissecting forceps and pulled down to expose the lower end of the internal hemorrhoid, which is grasped with a forceps The pedicles of the hemorrhoids are then grasped with forceps and pulled down until there is a ridge of pink mucous membrane between each hemorrhoid, thus forming the "triangle of exposure" (Fig 120) The left lateral hemorrhoid is removed first With a blunt scissors, a cut is made through the thin squamous epithelial lining of the anal canal and perianal skin, and another cut is made on the other side of the internal and external hemorrhoid the two incisions joining to make a V-shaped incision with its apex outward (Fig 121) The V-shaped flap is dissected inward, and the fine fibers of the longitudinal muscle passing to the skin are divided The flap of skin is dissected inward (taking with it the subcutaneous external hemorrhoidal plexus) until the inner edge of the lower rounded border of the internal sphincter is exposed The circular and the longitudinal muscle fibers found here must not be divided The dissected hemorrhoid is transfixed immediately below the inner edge of the internal sphincter and at the level of the triangle of exposure, using a round-bodied needle and no. 4 chromic catgut (Figs 122 and 123) The right posterior and then the right anterior hemorrhoid are treated in the same way

A complete bridge of tissue must be left between the three hemorrhoids (Fig 124) The three ligatured hemorrhoids are removed, leaving an adequate stump below the point of ligature The pedicles are returned into the anal canal Any redundant skin is removed Portions of the external hemorrhoid plexus can be removed if necessary Bleeding should be controlled by forceps pressure, and ligatures should be avoided Secondary hemorrhoids can be removed with the primary hemorrhoids or removed separately A proctoscope is passed into the rectum and withdrawn slowly to determine any constriction A portion of 1 in Paul's latex colostomy tubing 3 in long is inserted into the rectum Gauze dressings are not used in the anal canal If it was necessary to remove skin in the midline, the anal canal anteriorly or posteriorly, the edge of the internal sphincter muscle should be divided

External tags are removed if they are symptomatic, and local anesthesia is used

plexus can be treated by removing a portion of skin over the thrombus and evacuating the clots.

**Solitary Polyps of Colon and Rectum: Study of Inherited Tendency** in a large family group is presented by Ralph C. Richards and Charles Woolf<sup>4</sup> (Univ. of Utah), who comment that Utah, because of its unusual religious background, which sanctioned polygamous marriage for some 50 years, provides unique families of great size for investigation of human genetic problems. In one family 33% (6 of 18) adult offspring died from gastrointestinal cancer; four of the growths definitely originated in the large bowel. In attempting to correlate this with presence of adenomatous polyps of colon and rectum, 62 third generation children were examined by means of sigmoidoscopy and roentgenograms. Small adenomatous polyps of rectum or rectosigmoid were found in 31 (50%). Age and sex distribution of patients and character of lesions were similar to that in other reported studies of solitary polyps of the large bowel. Two of 12 fourth generation children examined also have polyps and 14 of 20 third generation patients re-examined after 12-18 months were found to have new lesions.

The findings strongly suggest a definite familial trait in occurrence of solitary polyps and adequately explain the high incidence of large bowel carcinoma in the original family. A form of dominant inheritance is suggested. This family apparently represents the first reported instance in which solitary or occasional discrete polyps of the colon and rectum have shown a hereditary tendency. The data strongly support the original hypothesis correlating a high incidence of benign polyps with the established family history of increased frequency of large bowel carcinoma. They also support the well established idea that benign polyps are precursors of most, if not all, large bowel carcinomas.

The importance of this study to the family group concerned is obvious. Theoretically, removal of all polyps in the benign stage should virtually eliminate carcinoma of the large bowel; practically, this is impossible. However, with two thirds of the third generation under careful follow-up study, the unstudied one third of the family should provide an interesting comparison in determining effectiveness of established treatment and control of solitary polyps.

(4) Am. Surgeon 22:287-294, March, 1956.



laxity of the anal musculature Hemorrhoids at first are reduced spontaneously after defecation but later require digital reposition External hemorrhoids are painful and tender Hypertrophy of the perianal skin folds, forming skin tags, may occur after prolonged chronic infection or thrombosis Diagnosis is made by inspection, digital examination and proctoscopy Sigmoidoscopy is necessary in all cases

Surgery is the only sure cure for prolapsing hemorrhoids The St Mark's technic for internal hemorrhoids follows

**TECHNIC**—With the patient in the lithotomy position the perianal skin tags of each of the three primary hemorrhoids is grasped with a pair of nontoothed dissecting forceps and pulled down to expose the lower end of the internal hemorrhoid, which is grasped with a forceps The pedicles of the hemorrhoids are then grasped with forceps and pulled down until there is a ridge of pink mucous membrane between each hemorrhoid, thus forming the "triangle of exposure" (Fig 120) The left lateral hemorrhoid is removed first With a blunt scissors, a cut is made through the thin squamous epithelial lining of the anal canal and perianal skin, and another cut is made on the other side of the internal and external hemorrhoid the two incisions joining to make a V shaped incision with its apex outward (Fig 121) The V-shaped flap is dissected inward, and the fine fibers of the longitudinal muscle passing to the skin are divided The flap of skin is dissected inward (taking with it the subcutaneous external hemorrhoidal plexus) until the inner edge of the lower rounded border of the internal sphincter is exposed The circular and the longitudinal muscle fibers found here must not be divided The dissected hemorrhoid is transfixed immediately below the inner edge of the internal sphincter and at the level of the triangle of exposure, using a round bodied needle and no 4 chromic catgut (Figs 122 and 123) The right posterior and then the right anterior hemorrhoid are treated in the same way

A complete bridge of tissue must be left between the three hemorrhoids (Fig 124) The three ligatured hemorrhoids are removed, leaving an adequate stump below the point of ligature The pedicles are returned into the anal canal Any redundant skin is removed Portions of the external hemorrhoid plexus can be removed if necessary Bleeding should be controlled by forceps pressure, and ligatures should be avoided Secondary hemorrhoids can be removed with the primary hemorrhoids or removed separately A proctoscope is passed into the rectum and withdrawn slowly to determine any constriction A portion of 1 in Paul's latex colostomy tubing 3 in long is inserted into the rectum Gauze dressings are not used in the anal canal If it was necessary to remove skin in the midline of the anal canal anteriorly or posteriorly the lower edge of the internal sphincter muscle should be divided

External tags are removed only if they annoy the patient, and local anesthesia is used Thrombosis of the external

plexus can be treated by removing a portion of skin over the thrombus and evacuating the clots

**Solitary Polyps of Colon and Rectum** Study of Inherited Tendency in a large family group is presented by Ralph C Richards and Charles Woolf<sup>4</sup> (Univ of Utah), who comment that Utah, because of its unusual religious background, which sanctioned polygamous marriage for some 50 years, provides unique families of great size for investigation of human genetic problems. In one family 33% (6 of 18) adult offspring died from gastrointestinal cancer, four of the growths definitely originated in the large bowel. In attempting to correlate this with presence of adenomatous polyps of colon and rectum, 62 third generation children were examined by means of sigmoidoscopy and roentgenograms. Small adenomatous polyps of rectum or rectosigmoid were found in 31 (50%). Age and sex distribution of patients and character of lesions were similar to that in other reported studies of solitary polyps of the large bowel. Two of 12 fourth generation children examined also have polyps and 14 of 20 third generation patients re-examined after 12-18 months were found to have new lesions.

The findings strongly suggest a definite familial trait in occurrence of solitary polyps and adequately explain the high incidence of large bowel carcinoma in the original family. A form of dominant inheritance is suggested. This family apparently represents the first reported instance in which solitary or occasional discrete polyps of the colon and rectum have shown a hereditary tendency. The data strongly support the original hypothesis correlating a high incidence of benign polyps with the established family history of increased frequency of large bowel carcinoma. They also support the well established idea that benign polyps are precursors of most, if not all, large bowel carcinomas.

The importance of this study to the family group concerned is obvious. Theoretically, removal of all polyps in the benign stage should virtually eliminate carcinoma of the large bowel, practically, this is impossible. However, with two thirds of the third generation under careful follow up study, the unstudied one third of the family should provide an interesting comparison in determining effectiveness of established treatment and control of solitary polyps.

(4) Am Surgeon 22:287-294 March 1956

The clinical implication of a familial trait in the origin of solitary polyps is important and indicates that a more adequate family cancer history should be obtained from patients with such polyps. Not infrequently, two or more members of a family have succumbed to large bowel carcinoma. In such a family it would seem just as advisable to advocate a family survey of adult members as to continue routine, long term follow-ups on the individual with known polypoid disease.

► [There can no longer be any reasonable doubt about a strong hereditary influence in cancer of the large bowel. This influence seems to operate through the formation of polyps first.—Ed.]

**Bowel Function after Colectomy for Cancer, Polyps and Diverticulitis** in 73 patients is described by Richard C. Lillehei and Owen H. Wangenstein<sup>5</sup> (Univ. of Minnesota). Of 55 patients with an initial diagnosis of carcinoma of the colon and/or polyps, 38% were found to have polyps in a portion of the colon that was believed, preoperatively, to be uninvolved. These polyps would not have been removed if the conventional hemicolectomy on the right, or the usual segmental colectomy on the left, had been used. In three patients, an unsuspected carcinoma was found in the section of colon removed. A second carcinoma of the colon developed, either simultaneously or successively, in 18.6%. Unsuspected cancer of the cecum was found in one patient who had colectomy for diverticulitis.

If not more than 30 cm. of terminal ileum is excised with the colon, bowel function postoperatively is usually quite normal. The hospital mortality rate (5.5%) for total or subtotal colectomy compares favorably with that for less extensive colectomies. If no ileum is excised, persistent diarrhea is practically nonexistent, preservation of the ileocecal valve assures normal function of the bowel. Cecorectal anastomoses are performed by choice when the diameter of the distal component of the anastomosis is large. The remaining ring of cecal mucosa can be inspected through the proctoscope.

Total or subtotal colectomy is acceptable for all lesions of the colon in which no ileum or a very short segment thereof, needs to be removed. The frequency with which important findings are uncovered suggests that total or

subtotal colectomy should become, under favorable circumstances, the operation of choice for cancers of the colon beyond the hepatic flexure. For cancers of the cecum and ascending colon in which less than 20 cm. of ileum is removed, the colon may be excised to the iliac colon or rectum without persistent diarrhea resulting. "Second-look" operations are indicated in patients with colic cancer who, at primary operation, have involvement of regional lymph nodes. Among 33 patients so treated, 17 were free of cancer at the second operation; 15 remained well, and 2 died of diseases unrelated to cancer. Of 16 patients with residual cancer at the first second-look operation, 5 (31.2%) no longer had cancer at successive second-looks. More years of observation are required before the true value of the second-look operation can be determined.

**Cecal Forms of Crohn's Disease.** François Eudel and Roger Viguié<sup>6</sup> (Paris) consider Crohn's disease easy to diagnose when the terminal ileitis extends to the cecum and the ascending colon. When the condition begins in the cecum but remains strictly localized, however, clinical and radiologic diagnosis is practically impossible. In the only two cases in which this type of development seems to have occurred—one from the literature and one reported by the authors—microscopic examination was needed to establish the diagnosis.

Woman, 26, complaining of digestive disturbances and abdominal pains, was found on radiologic examination to have a cecal obstruction. Koch's bacilli could not be recovered from the stools, but a positive skin reaction to tuberculin and the facts that the patient's father had died from pulmonary tuberculosis and that the patient lived with a sister who was under treatment for tuberculous disease led to a diagnosis of hypertrophic tuberculosis of the cecum. Antituberculous treatment for about four months produced no improvement in the abdominal pains, and the cecal obstruction—a small tumor—appeared larger and more fixed. At operation, the macroscopic appearance of the tumor and mesentery seemed to confirm the diagnosis of hypertrophic cecal tuberculosis, and right hemicolectomy was performed. Microscopic examination of the specimen invalidated the diagnosis of tuberculosis and demonstrated sclerotic and inflammatory lesions characteristic of Crohn's disease. The postoperative course was marked by chills, fever and the appearance of a fistula (remote from the anastomosis) that persisted for 1½ months. Two months after the patient's discharge, the symptoms returned. Medical

(6) Presse med 63 1846-1848, Dec. 25, 1955

treatment was ineffective, and a second operation was performed. The anastomosis was functioning well, but the ileum and mesentery showed the characteristic appearance of Crohn's disease in an active phase. The mesentery was infiltrated with procaine according to Forget's method, and the anastomosis with some 20 cm of colon and 1 m of healthy small intestine measuring from the end of the ileal lesions were removed. Continuity was restored by a wide side to side anastomosis. The postoperative course was uneventful and 18 months later the patient was in excellent condition and had resumed her normal activities.

In the case from the literature, that of a woman, 45 thought to have acute appendicitis, a limited intestinal resection was performed. Cure resulted that was maintained for 10 years without recurrence. The rarity of the condition and the difficulty of establishing an accurate diagnosis make it hard to set any definite rules for treatment. Acute abdominal symptoms and threatening stenosis, however, seem to warrant surgery. Wide resection, especially of the small intestine, after extensive infiltration of the mesentery with procaine, is apparently the best procedure for dealing with cecal tumors of undetermined origin.

**Surgical Management of Diverticulitis** is reported by Harry E. Bacon (Philadelphia) and Miguel A. Valiente<sup>7</sup> (Hato Rey, P. R.). Re-evaluation of surgical management of diverticular disease of the colon indicates greater need for preventive resection particularly because of low mortality and morbidity now possible through control of colic bacterial flora, improved nutritional control and electrolyte replacement. Preventive resection in recurring diverticulitis can generally be undertaken in one stage. Before surgery, the patient should be treated conservatively until acute infection has subsided. Rehabilitation is excellent in most patients, provided a liberal segment of bowel is removed. Left hemicolectomy with anastomosis of the distal transverse colon to the low sigmoid or rectosigmoid is recommended.

Special problems will persist despite preventive resection because in many patients diagnosis of diverticulosis or diverticulitis is not made until a surgical complication develops. Acute or sudden perforation of the colon can usually be managed by repair of the site of rupture and may or may not be accompanied by transverse colostomy. If the

bowel wall is friable, local repair is not recommended. If possible, exteriorization is the treatment of choice. If the bowel cannot be readily mobilized, the inflammatory area is drained by a Babcock sump drain, and transverse colostomy is performed. A neomycin solution (5 Gm in 500 cc sterile saline) is injected directly into the bowel lumen and flushed through the colon by gentle manipulation.

Fistulas are treated by resection of the diseased bowel and removal of the fistulous tract. The viscus penetrated by the fistula (usually the bladder) is repaired. If a patient shows preoperative evidence of active infection and inflammation, a three stage procedure is best and consists of transverse colostomy, resection and closure of colostomy. Three weeks to three months elapse between colostomy and resection.

Strictures are treated by resection. Ruling out of carcinoma is important, and because of its high incidence in diverticulitis primary resection rather than a three stage operation is the procedure of choice if inflammatory reaction and infection are minimal. Hemorrhage, usually severe and accompanied by shock generally can be treated conservatively, but each patient must be prepared for resection of diseased bowel when blood loss has been controlled.

Among 73 resections, mortality rate was 2.2%. Among the 11 partial cystectomies for repair of vesical fistulas no deaths occurred. Complete rehabilitation was achieved in 54 of the 73 patients. 51 were completely symptom free. 3 had mild periodic distress. One had severe periodic distress, and one had a recurrent vesicosigmoid fistula. Fourteen were lost to follow up.

Palliative treatment has been outmoded and is rarely indicated unless other debilitating circumstances preclude definitive management.

**Ulcerative Colitis** Selection of Cases for Surgical Treatment is reported by Richard B. Cattell and Bentley P. Colcock<sup>8</sup> (Lahey Clinic). Many patients formerly considered hopeless chronic invalids have been rehabilitated by ileostomy and colectomy. If these are done while the patient is in good condition mortality is low, whereas if the patient has chronic anemia, malnutrition and severe diarrhea, mortality is high. Mortality rate at the clinic after ileostomy

(8) S. Clin. North America 35:817-822 June 1955

and colectomy fell from 18% between 1928 and 1946 to 4.3% between 1947 and 1952

Modern ileostomy appliances (Fig 125) help in rehabilitation. Inconspicuousness of the modern ileostomy bag and elimination of the distressing consequences of odor and fecal soiling enable patients to return to former occupations and to resume normal family life and social activities.

Surgery should be considered for the following patients

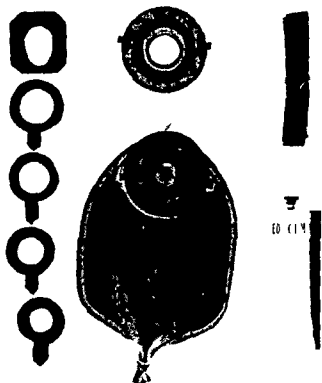


Fig 125—Torbot ileostomy bag. Rutzen and Perma type bags are similar. None projects more than 1.2 cm above level of the skin and all permit airtight water-tight union between disk and underlying skin. (Courtesy of Cattell, R. B. and Colcock, B. P. S. Clin. North America 35:817-822, June 1955.)

those unable to continue in normal occupations due to generalized weakness, those with constant severe diarrhea, those with a septic course, those with severe anemia, those with marked toxicity and severe bleeding, those with acute or chronic perforation of the bowel, those with obstruction, those with infectious arthritis, and, because of danger of carcinoma, those with ulcerative colitis for over eight years. Cortisone and ACTH give only temporary relief in presence of complications of chronic ulcerative colitis, only surgery can give permanent relief.

Perforation of the bowel in ulcerative colitis with generalized peritonitis must be treated conservatively with intubation and heavy doses of antibiotics before ileostomy can be performed. Any walled-off abscess must be drained. Ileostomy and colectomy are then performed when the condition of the patient improves.

Rehabilitation depends largely on a properly constructed, well functioning ileostomy. The modern ileostomy bag will not fit properly, and soiling of clothes will occur if the bag does not remain securely fastened. Prolapse, retraction, skin irritation and other complications can be avoided by careful attention to detail when the ileostomy is performed.

**Total Colectomy in Ulcerative Colitis**, with removal of the rectum, should be the ultimate goal in cases requiring operation, according to Laurence S. Fallis and James Barron<sup>9</sup> (Henry Ford Hosp.). Under ideal conditions, ileostomy, removal of the entire colon and resection of the rectum may be done in one stage. In other cases, graded procedures may be advisable. Ileostomy alone often is life-saving but should always be considered merely as a preliminary step. Removal of colon and rectum through an abdominal incision may be accomplished as follows:

**TECHNIC**—After exposure through a left pararectal incision extending from the costal margin to the pubic crest, the great omentum is carefully dissected from the transverse colon. The stomach with the attached great omentum is then pushed upward. Mobilization of the right colon is more difficult if ileostomy has been done, but is always facilitated by freeing the hepatic flexure first and then working downward to mobilize the cecum and terminal ileum. When ileostomy has not been done, section of the ileum is deferred until mobilization of colon and rectum is complete. The splenic flexure is mobilized from below upward after initial peritoneal incision in left colonic gutter close to ascending colon. The peritoneum of both surfaces of the sigmoid mesentery is cut close to the bowel margin for providing peritoneal flaps. The left ureter is protected. The superior hemorrhoidal artery is sectioned and ligated by transfixion at the promontory of the sacrum. The rectum and mesorectal fat are freed from sacrum, and the peritoneum is carefully peeled from the pelvic walls and margins of rectum and rectosigmoid before it is cut. Anteriorly, the rectum is separated from the bladder and prostate, or from uterus and vagina down to the superior surface of the levator ani. The urethra is protected by an indwelling catheter. The lateral rectal stalks are cut across, and the middle hemorrhoidal arteries ligated. Section of the iliorectococcygeus frees the backward curve of the rectum. The main colonic arterial trunks are cut and ligated by



transfixion The bowel is removed from the mesentery close to its margin to preserve as much peritoneum as possible As the right colon is separated from its mesentery, care is taken to protect the right ureter and duodenum A hernia tape is tied around the rectum just above the levator ani attachment With long curved scissors dissection of the lower rectum is continued distally until the levator attachments are entirely free i.e. when the ischiorectal fat is seen Traction and continued dissection separate the anal canal and perianal skin from the external sphincter muscles The perianal skin is cut across at right angles to the long axis of the rectum, thereby completely mobilizing the entire colon and rectum

This operation was carried out on 20 patients without a death Convalescence was rapid, since on large perineal wound was left to heal slowly All complications were due to difficulties associated with the ileostomy The complications have been lessened by using a separate opening with circular skin incision for ileostomy and immediate suture of ileal mucosa to the skin margin, as advocated by Brooke and Turnbull, and by application of the Rutzen bag in the immediate postoperative period

Preoperative correction of nutritional deficiencies by tube feeding (5,000-8,000 calories each 24 hours) for one to four weeks helped greatly in making the one stage procedure feasible

► [It is gratifying to see the excellent results from resection obtained to day as compared with the discouraging results of 20 years ago The surgical treatment of this condition has definitely become established Compare the following abstract on treatment by cortisone—Ed]

**Cortisone in Ulcerative Colitis** Final Report on Therapeutic Trial on 210 patients in 5 hospital regions is presented by S. C. Truelove and L. J. Witts<sup>1</sup> (Radcliffe Infirmary, Oxford) with the cooperation of others Cortisone (usually to 100 mg daily for six weeks) was administered to 109 patients and 101 received an inert preparation of similar appearance Physicians were not informed which preparation the patient was receiving

At every stage of severity of the illness and in both first attacks and relapses cortisone treated patients did better than corresponding controls Cortisone was particularly beneficial in first attacks Patients treated with cortisone were somewhat more likely to suffer from pyogenic complications than patients not so treated Among the cortisone-treated there were six cases of ischiorectal abscess and one diagnosed as pyoderma gangrenosa Among controls there

(1) *Brit. M. J.* 2:1041-1048 Oct. 29, 1955

were two cases of rectovaginal fistula (one accompanied by gross perianal infection) and one gangrenous appendix eventuating in pelvic abscess. Eye inflammations developed in three patients taking cortisone. It is probably wise to use penicillin or sulfonamides in addition to cortisone. With other complications, there was no significant difference in the two groups.

Sigmoidoscopy in 120 patients at the end of treatment showed more frequent normal or improved appearances in the cortisone group. Similarly, improvement in radiologic appearances was more common in patients who had received cortisone among 51 examined by barium enema at the end of treatment.

Of 16 deaths that occurred during treatment or within two months, 5 (46%) were among cortisone-treated patients and 11 in the control group (109%). Eight deaths occurred among the 24 patients subjected to ileostomy, 2 of them in the cortisone group.

Late follow-up information for an average of 18 months on 205 patients showed that 9 months after the trial period patients treated with cortisone in the first attack preserved a clear advantage over controls. By contrast, relapsed patients treated with cortisone had lost the initial advantage they showed at the end of the trial period. At the end of the follow-up period, essentially the same pattern existed but with a slight worsening of the general picture. About one fifth of the original group had been treated with ileostomy by the end of the study. Of these 44 patients, 14 (31.8%) were dead.

The authors conclude that cortisone is a valuable addition to medical treatment of ulcerative colitis. It is likely that better short term results might be achieved by use of higher doses when necessary. However, the effect of cortisone is far from permanent, particularly in established disease, though more prolonged treatment might give better long term results.

► [See the two preceding abstracts on the surgical treatment—Ed.]

**Biopsy of Rectum in Ulcerative Colitis** George Lumb and R. H. B. Protheroe<sup>2</sup> (Westminster Hosp., London) found the rectum involved in 137 of 150 patients with ulcerative colitis. Of the 137, 46.7% had radiologic evidence of

ulcerative colitis in the entire colon, whereas 53.3% had only the distal colon involved. In 19 of these no radiologic changes were found, and diagnosis was made by sigmoidoscopy and biopsy. In the other 54, radiologic changes were seen in the sigmoid, the descending colon or both.

The primary lesion of ulcerative colitis in the rectum consists of small erosions produced by breakdown of epithelial cells at the base of crypts, with subsequent formation of crypt abscesses and spread of the disease. In acute and severe cases, widespread ulceration develops, but chronic inflammatory exudate and some attempt at repair are nearly always seen. In milder cases, the lesions remain more localized, ulceration is not so severe and repair is more obvious. In 48 patients, the mucosa was intact, and the ulcerative colitis appeared to be quiescent. The essential lesion of ulcerative colitis seen in rectal biopsy material seems to be excessive destruction of undifferentiated cells in the crypts leading to failure of repair and to subsequent secondary infection.

The mechanism of formation and rupture of crypt abscesses is of importance in understanding the etiology of ulcerative colitis. Unknown factors cause death of the mucosal cells in the crypts. Study of the crypt abscesses reveals pale staining vacuolated cells undergoing necrotic change, actual breakdown of epithelial continuity and foci of repair by flattened epithelial cells. It is postulated that neutrophils are attracted by chemotactic influences originating from the damaged cells or from organisms in the crypt lumens. Other possible factors include an allergic inflammatory origin, parasympathetic hyperactivity which may originate from psychogenic stimuli and some local surface irritant of enzymatic type, such as mucinase. It is possible that no single cause of ulcerative colitis exists but that some intrinsic failure of normal regeneration of epithelial cells may be aggravated by several extrinsic factors.

**Management of Cecal Cancer Discovered Unexpectedly at Operation for Acute Appendicitis.** Howard A. Patterson<sup>3</sup> (Roosevelt Hosp., New York) states that a cecal cancer can block the base of the appendix and cause symptoms of acute appendicitis before other symptoms of the cancer are manifested. The result may be delay in obtaining the true diag-

nosis, multiple operations and poor prognosis. The large lumen and fluid content of the cecum contribute to the lack of symptoms until the cancer is large. The usual pattern is that an operation is done for acute appendicitis, with or without abscess, and a fecal fistula follows which closes in about four weeks. About four months after the first operation, the patient returns with an abscess, a mass, or both and is likely to have carcinoma growing along the old drainage tract. The diagnosis may be missed even in the second operation, particularly with a recurrent abscess.

If an unexpected cecal cancer is present with acute appendicitis the decision regarding the procedure of choice depends on the extent of peritoneal involvement. In the presence of a large foul abscess, drainage alone may be best as a preliminary procedure. Otherwise, the alternatives include side to side ileocolostomy, with plans for resection later; division of the ileum and ileocolostomy (performed by either bringing the terminal ileum out as a fistula or turning it in), or primary resection even in the presence of peritonitis. The last is the best procedure for cure of the cancer. Since few hepatic flexures are at a high level ample access for adequate resection can usually be obtained by extending a McBurney incision medially across the right rectus muscle and sheath. It is unwise to extend it laterally and upward, the small incision can be closed and a large one made.

The ileocecal region is notorious for inflammatory masses that may be difficult to distinguish from carcinoma. *Recurring right lower quadrant pain with tenderness, closely simulating appendicitis* may be due to obstructing colonic cancer even at a site remote from the cecum. The cecal cancer, often bulky, ulcerated and of long standing when discovered, may present the typical history and physical findings of acute appendicitis, with subsequent exploration revealing a perfectly normal appendix. The surgeon must make a thorough examination when exploring for acute appendicitis, especially in older patients.

Of about 200 patients with cancer of the right half of the colon 72 had the cancer in the cecum and in about one fourth the acute inflammatory features dominated the clinical picture. The base of the appendix was blocked by cecal cancer with resulting appendicitis, in 13. One of the tu-

mors was a malignant carcinoid, the others were of the usual type. The correct diagnosis was made at the first operation in seven cases, whereas in six the true diagnosis was not made until a total of 12 operations were made. The prognosis as a whole was poor.

Cancer of the Colon is more adaptable to extirpation than cancers in many other locations. Arthur W. Allen, Claude E. Welch and Gordon Donaldson<sup>4</sup> (Massachusetts Gen'l Hosp.) report a group of private patients, personally treated, to demonstrate that with a high resection rate and low operative mortality a higher salvage rate may be expected. Average time from onset to admission was 45 months, while in all patients treated at the hospital it was 7 months and, among the latter, resection and five year survival rates were significantly lower. Apparently, about 80% of patients with negative nodes may be cured, 20% eventually die of liver metastases. Positive lymph nodes reduce cure rate by about half.

If local nodes are firm and apparently invaded by tumor, resection should be as radical as is compatible with life, provided the liver is not involved. Cure rate can be materially increased by block resection of all feasible contact or directly involved structures. Extending the resection to include two or more segments of bowel is sometimes justifiable. When segmental lymph nodes are apparently involved, it often is necessary to remove the entire blood supply to the left colon and to anastomose the transverse colon to the rectum; however, routine use of this procedure in all lesions of the left colon is debatable. Patients surviving resection should be observed periodically the rest of their lives. Some individuals return with remediable lesions at least once and sometimes twice. When the original operation is as radical as is feasible, manifestations of further trouble should be awaited before advising another operation.

**PROCEDURE**—When obstruction is not complete (about 96% of patients in this series) a minimum of five days is invested in proper *preoperative preparation including cardiac evaluation and protection, correction of anemia by blood transfusions and of biochemical deficiencies, determination of bleeding and clotting times and prothrombin levels, along with local preparation of the bowel.* Sulfathiazole<sup>®</sup> 8 Gm, is given daily for five days before large bowel resection.

(4) West J Surg 63:355-361, June 1955

Cultures of bowel are obtained routinely at operation, and staphylococcus organisms are titered against available antibacterial agents. In complete left bowel obstruction, preliminary decompression by tube cecostomy is safest; this may sometimes be followed by transverse colostomy, usually safe for decompression when distention of cecum is slight and diameter of transverse colon is less than 10 cm. Delay of 7-21 days for transverse colostomy before resection of the primary lesion in obstructed cases is a small price to pay for the added safety produced.

Operations are performed under gas-oxygen-ether through an intratracheal tube, and approaches are carefully planned to preserve nerve and blood supplies of the abdominal wall. Incisions must be adequate for complete exposure of area to be sacrificed, with minimum trauma to small intestine. End-to-end open anastomosis is used routinely. The abdominal wall is repaired carefully.

Meticulous after-care is important. Intravenous saline and 5% dextrose, potassium chloride, 60 mEq. and soluble vitamins B and C, transfusions, anticoagulants routinely, leg exercises, elastic stockings, elevation of the foot of the bed, early ambulation (second day), adequate sedation, and streptomycin and penicillin for five days are recommended. Bowel movements occur spontaneously on the fourth to seventh day. The rectum is examined daily after third day to prevent impactions.

Resection rate in 323 patients in a 10 year period was 96.6%. Palliative resections were done in 50 patients (15.5%) with liver metastases or widespread peritoneal involvement, with survivals to 4½ years (average 9 months). The 262 resections for cure (81.1%), included 64 (of 76) with contact spread. Operative mortality in this group was 2.3%; in the palliative group, 14%; and 36.3% in those with nonresectable lesions, despite minimal procedures performed. Five year salvage in all cases, including nonresectable and palliative cases and operative deaths, was 46.8%. Eliminating operative deaths, the five year cure rate in 153 consecutive patients resected with hope of cure was 66%.

**Carcinoma of Right Side of Colon: Operability, Resectability and Survival Rates.** George D. J. Griffin, Edward S. Judd and Robert P. Gage<sup>5</sup> (Mayo Clinic) compared all surgically treated patients with carcinoma of the right side of the colon seen from 1939 through 1948 with a 1907-38 series previously reported. In the later series there were 373 males and 273 females. Slightly more than 90% of the patients were over 40 and over half were between 50 and 70. The cecum was involved in 47.2%, ascending colon in 30.2% and hepatic flexure in 22.6% Metastases to regional lymph

(5) Ann. Surg. 143:330-336, March, 1956.

nodes were found in 48.1%. There was no unusual tendency for lesions in any one anatomic location or of a particular grade of malignancy to metastasize.

The records of all surgical cases of carcinoma of the right colon seen in 1952 were also reviewed. The operability rate in 1952 was 94%. Rate of "curative" resections in 1939-48 was 70.3% and was essentially unchanged in 1952. The over-all resectability rate increased from 67 to 77.1% in the 1939-48 series and to 85.9% in 1952, because of the increasing use of palliative resection. The percentages of the various types of operations in the 1939-48 group and in 1952 were "curative" resection 70.3% and 70.5%, palliative resection 6.8% and 15.4%, ileocolostomy 18.6% and 12.8%, and exploration 4.3% and 1.3%.

The hospital mortality rate was 6.5% for the 1939-48 series, 6.4% in 1952 and 23.5% in 1907-38. In 1938-48 the greatest mortality was after ileocolostomy operations.

The five year survival rate of patients undergoing resection with a view to cure in the 1939-48 group was 60.4%, compared with 57% in the 1907-38 group, suggesting that fundamentally the situation has not improved greatly in recent years. However, because of the difference in hospital mortality rates and perhaps in operability rates, more patients now survive carcinoma of the right portion of the colon than before 1939. This advance is based primarily on adjuncts to surgical care and acceptance of the one stage radical hemicolectomy as the procedure of choice when cure is the object and in many instances when palliation is desired. Palliative resection involves only slightly more risk than does palliative ileocolostomy and benefits the patient much more.

Treatment of Cancer of Rectum is discussed by E. G. Muir<sup>6</sup> (King's College Hosp. London). Cancer of the rectum can spread laterally in the lymphatics and upward along the inferior mesenteric artery and dissection of the lateral pelvic walls is necessary in all low rectal growths. Some surgeons advocate dissection and clearance of the para-aortic glands from the duodenum downward and ligation of the inferior mesenteric artery at its aortic origin. Others advocate re-exploration six months after the first operation and before any clinical evidence of recurrence is

(6) Ann Roy Coll Surgeons England 17:48-57 July 1955

noted, in patients with lymph node involvement found at excision of growth

Venous invasion is frequent. Not all patients with venous invasion will have metastases, but prognosis is worse. Venous invasion is commoner in advanced and highly malignant growths. The liver is the commonest site for visceral metastases, but the lung is commoner than supposed. Liver metastases suggesting only short life expectancy contraindicate excision, even if the growth is small and mobile, and also palliative colostomy unless essential. Early metastases and an operable growth indicate excision, for life with an advanced rectal growth is miserable. Metastases sometimes grow slowly, and a hemangioma or adenoma in the liver may be mistaken for a secondary deposit. Excision seems justifiable for a solitary metastasis in the liver.

Rectal cancers above and below the peritoneal level may involve by direct invasion the adjoining pelvic organs. The primary growth, with the uterus and adnexa and the posterior vaginal wall can be removed. Parts of the bladder and the small bowel can also be removed with the primary growth. The hazards of operation are increased if the bladder base, vesicles, prostate and ureters are involved when the case must either be regarded as inoperable or the entire pelvis cleared of its contents.

The standard operation in radical treatment of rectal cancer is some form of combined excision. In some instances, anterior resection is justified and some patients can be treated by perineal excision and Hartmann's abdominal resection. The combined excision can be performed by the abdominoperineal, the perineoabdominal or the synchronous combined routes. Results vary with operability rate, stage of growth and lymphatic spread and venous invasion and histology. Operability rate is as high as 80%. Operative mortality is 5-10%. The over all five year survival rate, after combined excision, is around 50%, with over 80% for early, well differentiated growths and 30% or less for growths with lymphatic involvement.

Radical removal of the rectum with preservation of the sphincter may be performed from the abdomen alone or by a combination of the abdominal and perineal routes. In the former the anastomosis between the end of the sigmoid



the rectal stump is made in the depths of the pelvis; in the latter, it is made in the perineum, either posterior to the anus, after partial division of the levator ani muscle, or outside the anal canal. If it is to be effective in radical treatment, the anterior resection operation should include ligation of the inferior mesenteric artery below the first sigmoid branch or at its origin from the aorta; a clear margin of 5 cm. of bowel must be removed below the growth; 5-6 cm. of rectal stump should be left behind; the remaining rectal mucosa must be free from adenomas; the sigmoid colon must reach the rectal stump without strain and with a good blood supply, the growth should be of early and not of high malignancy, and the operation should not be performed in obese patients. Final decision on the type of surgery is made during surgery. Restorative resection is a palliative operation for patients with a locally operable growth but with hepatic metastases.

Recurrences may appear in or near the anastomotic line of the rectal stump due to implantation of cancer cells, lying in the lumen of the bowel at the time of resection, in the anastomotic line, or to the stimulus of repair, exciting a fresh growth in a precancerous bowel. Survival rate is higher after anterior resection than after a combined operation because the lesions are usually less malignant.

Hartmann's operation, which consists of mobilizing the rectum as for a combined excision and resecting it, leaving a small rectal stump which is oversewn, the patient being left with a terminal colostomy, is used in frail patients; recurrence rate is high. Perineal resection is not a satisfactory operation because the lymphatics cannot be removed. It is useful only for palliation.

**Technical Considerations in Sphincter-Preserving Operations for Rectosigmoid Area.** According to R. Russell Best<sup>7</sup> (Univ. of Nebraska), not all patients with carcinoma of the rectosigmoid area need a radical abdominal perineal operation with a permanent colostomy. If the lesion is 5 cm. or less from the external sphincter margin, a sphincter-preserving operation is not possible and an abdominal perineal resection and permanent colostomy are indicated. For lesions between 5 and 10 cm. levels and for all lesions found below the peritoneal floor on exploration, a radical abdominal dis-

section followed by posterior resection and anastomosis is recommended. The lower level of transection should be at least 5 cm below the lower margin of the tumor, in most patients, just above the sphincter level. The accompanying colostomy of the transverse colon is closed in 8-10 weeks. For lesions which are above the 10 cm level and, on exploration, are at or above the pelvic peritoneal floor level, dissection, resection and anastomosis are accomplished entirely from within the abdomen. This procedure is accompanied by a cecostomy, using a mushroom catheter, which is removed after the patient has had bowel movements for several days. A drain is kept in the pelvis through a small incision in the perineum, for a few days.

Some posterior fecal drainage occurs in 20% of the patients with the perineal sphincter-preserving operation, compared with 10% of patients with the abdominal sphincter preserving operation. Potassium permanganate irrigations and hot sitz baths help close the fistulas. Anastomotic areas will tend to contract, and frequent rectal examinations and periodic rectal and anal dilatations may be necessary.

Of 130 patients with carcinoma of the rectum, rectosigmoid and lower sigmoid 93% were operable, 82% had colostomy only, 24.3% an abdominal perineal resection and 75.6% an anastomosis with sphincter preservation. The mortality rate of the 121 operated patients was 7.5%, of those with colostomy only, 30%, with abdominal perineal resection, 37%, and with an anastomosis operation, 5.9%. Local recurrence occurred in 7 out of 84 patients who had a sphincter saving operation and an abdominal perineal resection was subsequently performed in 4. The three and five year survival rates in the resection and anastomosis groups is comparable to the abdominal perineal resection group.

Sphincter control was adequate in all patients with the sphincter saving operations. Sexual potency was retained in about 80% of the patients compared with 10-15% following the abdominal perineal resection.

**Anterior Resection of Rectum** was performed by Edward Wilson<sup>8</sup> (Sydney, Australia) in 28 (19 males) of 114 patients (24.5%) with excision of rectal carcinoma. In six, the operation was merely palliative. The uterus also had to

be removed in three, the left ovary in two and a loop of ileum in one. In general, final decision as to the suitability of anterior resection should be postponed until the abdomen has been opened. Besides its use to cure rectal cancer, anterior resection is indicated in some patients with a few hepatic or peritoneal metastases and in some who refuse an abdominoperineal procedure or who would be unable to manage a colostomy. This operation was also performed in nine cases of diverticulitis and single cases of villous papilloma, endometriosis, familial polyposis and involvement of the upper rectum by an ovarian cancer. Preliminary colostomy on the right side of the transverse colon was necessary in some patients, in others, resection was performed in one stage after administration of phthalylsulfathiazole and oral streptomycin.

**PROCEDURE**—When preliminary colostomy is used, a sutured spur is usually constructed; this is subsequently crushed with an enterotome, with closure later. Anastomosis deep within the pelvis within reach of the examining finger is recommended. The colon is sufficiently freed to allow it to lie without tension at the suture line. This also avoids pressure and possible thrombosis of vessels at the pelvic brim. In operating for a benign condition, less lymphatic field is removed and the main trunk of the superior hemorrhoidal vessels may be preserved. Ligation of these vessels, however, causes no sloughing of the lower rectal stump, which is supplied from branches of the middle and inferior hemorrhoidal vessels. The possibility of local recurrence is minimized by irrigation of the lower bowel with 1:500 perchloride of mercury by application of clamps at least 2 in. below the growth early in operation and by not using anterior resections for large, low, fixed growths. If a growth is unusually friable, its surface is fulgurated before beginning the operation.

In this small series, there were no recurrences at the suture line. In five patients (two with carcinoma, three with diverticulitis) a fecal fistula developed along the track of the tube but healed spontaneously. Within a three year follow-up, five patients died, four of whom had palliative operations.

**Lateral Spread of Carcinoma of the Rectum**, along lateral rectal vessels draining to the iliac chain, has not been adequately studied, according to J. Freidin<sup>9</sup> (Univ. of Melbourne), in contrast to the upward lymphatic spread along superior rectal vessels and the downward spread below the tumor. Most authors believe that the slightly poorer prognosis with low lying rectal neoplasms following abdomino-

(9) Australian & New England J. Surg. 24:285-294, May 1955.

perineal resection of the rectum is due to spread via the lateral vessel route as well as through the superior route. Former attempts to demonstrate the lateral route have been unsuccessful or have shown evidence of lateral spread only in tumors with complete blockage by metastases of the superior route.

A careful anatomic dissection of 100 specimens of carcinoma of the rectum and sigmoid colon removed by an abdominoperineal resection was performed. The gross dissection included a careful search for lateral hemorrhoidal vessels and a histologic examination of related lymph nodes. These vessels and lymph nodes are contained in the lateral vascular bundle, the so called lateral "ligament," which is the mass of fibrofatty tissue that holds the rectum in the pelvis after the peritoneum and superior vessels above and the levators below have been thoroughly divided. The superior hemorrhoidal vessels were also dissected to aid in demonstration of the lateral vessels. Some specimens contained no lateral vessels.

The specimens were divided into three groups according to their level in relation to the lateral vessel fields of spread. Of 13 tumors below the lateral vessel fields, 5 showed lateral vessels and 2 had related lymph nodes involved by neoplasm. Of 48 tumors situated at the level of the lateral zone, 34 had lateral vessels and 18 had related lymph nodes. Neoplasm was found in the lateral lymph nodes of 10. In these two groups lateral spread occurred despite a superior avenue of spread that was either free of metastasis or contained only a small amount. Of 39 tumors above the lateral fields, 23 had lateral vessels but only 4 had related lymph nodes, none of which contained neoplasm.

The study demonstrates that carcinoma of the rectum can spread laterally along the lateral rectal vessels whether the tumor is below or at the same level as the lateral vessels and may be present when the superior route of spread is still uninvolved.

**Implantation of Tumor Cells as Factor in Recurrence of Carcinoma of Rectosigmoid.** Oliver H. Beahrs, John W. Phillips and Malcolm B. Dockerty<sup>1</sup> (Mayo Clinic) reviewed the records of 1,796 patients operated on for carcinoma of the sigmoid, rectum or anus to re-evaluate the problem of

(1) *Cancer* 8:831-838, July-Aug. 1955.

hemorrhoidectomy and symptomatic anorectal treatment as well as to find cases in which implantation seemed to have played a role in the appearance of recurrent carcinoma below the primary lesion. No attempt was made to investigate recurrence at the suture line following anterior resection. The histories showed that 128 (71%) of the patients had undergone surgical or symptomatic treatment of hemorrhoids during the period of symptoms of carcinoma of the large bowel. Hemorrhoidectomy had been performed in 78 cases, and 50 patients had received suppositories, ointments or other symptomatic treatment.

In four cases, recurrent carcinoma developed at the dentate line. These appeared to occur on the basis of implantation of malignant cells via the fecal stream onto raw surfaces of granulation tissue resulting from hemorrhoidectomy or other anorectal operation. The preserved surgical specimen was studied in great detail in these cases. Sections were made from the primary lesion, pericolic tissue and regional lymph nodes, recurrent growth at the dentate line and the wall of the bowel between the two growths. A thorough attempt was made to exclude the possibility of multiple primary growths, malignant degeneration of hemorrhoids or extensive retrograde intramural or lymphatic spread.

All four of these patients had rectal bleeding or pain as an early symptom. In two cases hemorrhoidectomy had been performed and in the third case this procedure had been recommended before diagnosis of carcinoma of the bowel. The fourth patient had also been treated for hemorrhoids before diagnosis. In all four cases, a secondary carcinoma developed at the dentate line during the course of treatment.

These cases emphasize the danger of overlooking a carcinoma of the colon on the basis of rectal bleeding believed to be caused by hemorrhoids. Drop metastases with seeding of carcinoma cells on the raw granulating surfaces or bleeding hemorrhoids are the most likely explanation for the secondary tumors in the four cases cited. The frequency of implantation of desquamated malignant cells onto raw anal surfaces is unknown. However, this study indicates that successful survival of the seeded malignant cells is suffi-

ciently infrequent to be clinically important only in occasional cases

► [These important findings ought to become known to those who are too quick to operate for supposed hemorrhoids—Ed]

**Diverticulitis of the Colon** Leo Friesen and Erwin R. Schmidt<sup>2</sup> (Univ of Wisconsin) reviewed the records of 301 patients (170 women) with diverticulitis or diverticulosis and found that surgery was necessary in 9 women and 13 men. Antibiotics have allowed a more conservative approach to the management of diverticulitis in the acute inflammatory phase and a more radical attack on the chronic obstructive phase. Chronic obstructive diverticulitis due to stenosis is the commonest indication for surgery. Conservative surgery is best for the uncomplicated form.

There is a lack of agreement on the best surgical procedure for complicated diverticulitis. The safest operation is a colostomy proximal to the lesion to divert the fecal stream completely, after which sufficient time is allowed for the inflammatory reaction to subside before attempting further surgery (usually six months to a year). If carcinoma is suspected, surgery should not be delayed. Factors influencing the choice of surgery are age and general condition of the patient, acuteness of the process, presence or absence and degree of obstruction, number and duration of previous attacks, extent of inflammatory reaction, presence or absence of a fistula or abscess and mobility and accessibility of the involved segment of sigmoid.

Primary resection with end to end anastomosis was performed in nine patients, seven with chronic stenosing diverticulitis, one with massive hemorrhage and one with a pelvic mass. Symptoms included recurrent crampy left lower abdominal pain, gross blood in the stool, diarrhea, constipation, narrowing of stools and weight loss. X-ray findings indicated carcinoma in two. There were no deaths. One patient had a temporary leak at the anastomosis. A three stage procedure, consisting of a colostomy followed by resection and later closure of the colostomy, was used in three patients, two with acute bowel obstruction and one with a severe inflammatory reaction. Time between colostomy and resection was 4, 10, and 11 months, respectively, and time between resection and closure of colostomy was 6, 3 and 8

months One patient had postoperative wound dehiscence. All survived. A two stage procedure, consisting of preliminary transverse colostomy followed later by resection and closure of the colostomy at the same time, was performed in two patients, one with a large pelvic mass and one with a vesicocolic fistula. Interval between operations was four and eight months. There were no complications.

In one case the involved sigmoid colon was exteriorized and resected and the resulting colostomy closed three months later. The patient had a temporary leak at the anastomosis. Ileosigmoidostomy was performed in a patient who was too unco-operative for more extensive surgery. A permanent colostomy was performed in one patient with advanced heart disease and a transverse colostomy followed by closure without resection in a patient with an abscess. Drainage only and cecostomy only were performed in one patient each. Drainage of a pelvic abscess with transverse colostomy was performed twice. Both patients died, one of infection and shock and the other of obstruction.

**Some Clinical Aspects of Factitial Proctitis: Report of 62 Cases** occurring among 159 patients irradiated for gynecologic pelvic malignancies is presented by Bernard J Kaplan<sup>3</sup> (Univ. of Minnesota). Deep x-ray therapy or radioactive cobalt therapy followed by intracavitary radium application was used. Occurrence of proctitis after irradiation does not mean that faulty technique was used and that it must be considered a definite risk whenever the pelvic area is irradiated. The actual incidence may be higher than the 15.59% recorded, since over 30% of patients may have mucosal changes but no symptoms. Symptoms may appear any time up to five to seven years or more after irradiation, and any patient with or without bowel disturbances after irradiation should be suspected of having factitial proctitis and should be examined by proctoscope.

The proctoscopic picture is characteristic. Telangiectasia is present in all grades of proctitis, from the earliest mild cases to the most severe chronic ones, as well as those designated as 'healed'. The earliest changes appear as mild to moderate erythema with some mucosal edema. With progression, the surface of the bowel, usually on the midanterior rectal wall appears to be covered with a pale, stellate-

shaped membrane, with a surrounding area of inflammation. This area eventually becomes eroded and progresses to ulceration. The mucosal edges of the ulcer are inflamed and telangiectatic and bleed easily. If healing occurs at this stage, the base becomes less depressed and the ulcer becomes smaller by inward growth of the mucosal edges; ultimately, a pale, stellate scar with surrounding telangiectasia remains. If proctitis progresses still further, all rectal layers become involved with an inflammatory reaction, giving the wall a thickened appearance, with resulting stenosis and stricture formation. Occasionally an ulcer will continue to penetrate through the anterior rectal wall until a rectovaginal fistula results. The fistula edges may appear heaped up and firm, making differentiation from infiltrating carcinoma difficult.

In this series, proctitis in most cases was relatively mild. Therapy usually consisted of twice daily rectal applications of 75 mg. of 2.5% hydrocortisone acetate for eight consecutive weeks. In a few cases with extensive involvement, the treatment period was lengthened to 12 weeks. Pronounced improvement was generally noted after two to four weeks; after eight weeks often only a superficial scar remained. The surrounding mucosa often appeared quite normal except for occasional telangiectasia. In some cases it appeared granular and telangiectatic, but in all the inflamed and edematous appearance of the mucosa disappeared. In cases with rectovaginal fistula treatment produced similar changes in the mucosa about the fistula edges, but there was no change in the size of the fistula. If untreated, lesions of factitial proctitis will heal gradually in 12-24 months.

In over 90% of patients either healing or improvement followed treatment. In one with a large rectovaginal fistula no change occurred after 12 weeks of therapy. Two patients were made worse, in that rectovaginal fistulas developed. These probably would have occurred anyway, especially since one patient was treated with hydrocortisone for only one week and the other for about two weeks. These are reported as being due to therapy, for the occurrence of bowel perforation with hydrocortisone is a definite possibility and should be kept in mind. The effect of hydrocortisone appears to be purely local, since there were no signs of significant absorption.



**Sigmoidorectomyotomy for Hirschsprung's Disease.** According to Max Saegesser<sup>4</sup> (Bern), total colectomy and sigmoidorectal resection, previously recommended in treatment of Hirschsprung's disease, are extensive and dangerous operations that do not deal with the real cause of the disease. Under normal conditions, the intestine is contracted under influence of sympathetic stimulation and dilated by vagal action. Removal of the vagal reflex leaves the colon contracted. This explains the absence of mural thickening due to muscular hypertrophy in the stenosed portion of the intestine. The intestine is narrowed because it lacks the power

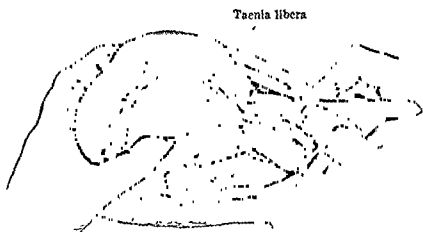


Fig 126—Taenia is split above the stenotic portion as far as fold of Douglas. (Courtesy of Saegesser, M : *Chirurg* 25 175-176, April, 1954 )

to dilate. In the constricted sigmoidorectal segment, ganglion cells of Auerbach's plexus are decreased or completely absent. That the condition is not due merely to spasm is evident because proximal dilatation and elongation of the colon is much greater than in organic or spastic stenosis. Hence the possibility of imbalance in the sympathetic-parasympathetic neural mechanism cannot be disregarded. Similar conditions seen in idiopathic cardiospasm with megaesophagus suggested the feasibility of sigmoidomyotomy similar to Heller's cardiomyotomy.

This operation has been performed on two girls, 13 and 15, with severe megacolon. X-rays in both cases exhibited an area of transition between the highly dilated sigmoid and the stenotic portion of the rectosigmoid. In the older girl, cecostomy had been performed several times during attacks

(4) *Chirurg* 25 175 176, April, 1954

of ileus. For three weeks after operation both patients had spontaneous evacuation of massive quantities of feces. During the following month, bowel movements became normal. Both patients remained well, for 13 months and 2 years, respectively, since operation.

Technic of sigmoidorectomyotomy is simple. The sigmoid loop is exposed by a left-sided pararectal incision. In the region of transition between the dilated and contracted portions, the anterior taenia is split down to the mucous membrane (Fig 126), from a hand's breadth beyond the stenotic area approximately to the fold of Douglas. Mucous membrane must be exposed throughout. The sigmoid loop is then shifted medially, to expose the posterolateral taenia, where another incision is made, extending upward to the mucous membrane. At the end of the operation the anal sphincter is dilated carefully.

In contrast with other procedures used in Hirschsprung's disease, sigmoidorectomyotomy is easily performed and requires no sacrifice of intestine. On the basis of the results in two cases, the procedure is recommended in all cases in which conservative therapy has proved unsuccessful.

► [In 1950 I performed a similar operation on three children. In only one was there a successful result. The condition of Hirschsprung's disease cannot be properly compared with the mega esophagus for which Hellar's operation of myotomy is practically always successful.—Ed.]

---

## PILONIDAL CYSTS AND SINUSES

**Pilonidal Cyst Misnamed, Misunderstood and Mistreated**  
According to Robert M. Hardaway<sup>5</sup> (M C, U S A), pilonidal cyst is a tremendous military problem. During World War II (1942-45) 77,637 Army patients were treated for pilonidal disease and 3,387,000 man days were lost, representing a cost of over one hundred million dollars. Besides 9,000 patients admitted for other illnesses also had pilonidal sinus. The rate per thousand has increased from 3.05 during World War II to 3.24 during 1953, when 4,955 were treated for pilonidal disease, with loss of 121,000 man-days.

A follow-up showed that although initial results of surgical excision in most properly prepared patients were fairly

(5) U. S. Armed Forces M. J. 7:516-522, April 1956.

good, a large proportion had further trouble. Attempts to obliterate dead space, preserve normal tissue, cover the sacrum with fat-padded skin, eliminate buried suture material and other good surgical principles seemed to have no dramatic effect.

The disease is congenital, the tract is an epithelium-lined sinus, possibly resulting from defective closure of the neural groove. The time (after puberty) of initial infection of the tract and frequent "recurrence" after adequate excision point to ingrowing hair as a major problem. Even in normal persons with no congenital sinus, poor personal hygiene, sweat and irritation will produce a painful, tender inflammation in the intergluteal fold. As infection in the depths of the sinus progresses, it crosses and destroys the epithelial barrier and enters the fatty, subcutaneous, episcapular tissue, invoking a fibrous reaction in the fat and producing the so-called "pilonidal cyst," which is, in fact, a granuloma at the end of the sinus tract.

A conservative regimen recommended for treatment of military personnel with pilonidal disease includes meticulous personal hygiene, with soap and water (or hexachlorophene detergent) cleansing of intergluteal area daily, weight reduction, if necessary, upright sitting with no slouching on the sacrum, shaving of intergluteal area when infection is present or threatens, especially in summer, no assignment as drivers or routine passengers in a vehicle, incision and drainage of abscesses, sitz baths, broad spectrum antibiotics, curettage and/or minor excisions, in certain cases.

Definitive surgery is reserved for the few who fail to respond to adequate trial of conservative measures and who are, and intend to remain in, regular service. Excision should be done only after drainage and inflammation have been controlled and only diseased tissue removed. The patient should be informed that his chances of having subsequent trouble are altered little by operation and that relapses are best avoided by careful adherence to the advised regimen. Actually, the most difficult cases to control involve patients who have had previous excision.

► [Wonder what the author means when he recommends that only diseased tissue be removed. If the incised epithelium and hair are not removed, recurrence of trouble is practically sure to occur. Many of the failures of treatment during World War II were due to attempts to de-

vise fancy operations of various kinds that neglected to remove all of the involved epithelium—Ed.]

**Pilonidal Sinus Analysis of 206 Operations Performed According to Varying Technics** The literature on surgical treatment of pilonidal sinus presents varying statistics and opinions. Reported series range from no recurrences to 38% unsatisfactory results. Surgeons who favor primary suture believe that recurrences should be no greater than with open operation and stress that special care is not required after discharge from the hospital. Those who favor some type of open operation believe that recurrence rates are lower, complications fewer and hospitalization shorter than with the closed technic, and they tend to minimize the inconvenience of an open wound.

In an attempt to discover important factors which determine the statistical variation, David V. Pecora and Philip Cooper<sup>6</sup> re-examined 200 patients (6 had had two operations) operated on at the V. A. Hospital, Providence, R. I., from June 1949 to January 1953, and analyzed the historical, clinical and surgical data.

Preoperative and postoperative care were fairly well standardized. Patients with acute infection were treated by incision and drainage, sitz baths and antibiotics as indicated. Definitive operation was performed only when all acute inflammation had subsided. The skin of the sacral region was carefully cleansed preoperatively. Type of operation was decided by the surgeon at time of surgery. In both open and closed procedures block dissection was usually employed. Flaps were rarely created. Closure was almost invariably effected by burying absorbable (gut) sutures, rarely silk or wire. To obliterate dead space, skin was carefully approximated with nonabsorbable (silk) mattress sutures. After open operations the patient was ambulatory usually on the first postoperative day. After the first few days daily dressing was done and every effort was made to allow granulation to proceed from the depths of the wound. After primary suture, the patient was confined to bed and instructed not to lie on his back or flex his thighs for 10 days to 2 weeks. The first dressing was done about four days postoperatively. Thereafter in uncomplicated cases, ambulation was allowed. Infected wounds were opened wide and

(6) A. M. A. Arch. Surg. 71:752-755, November 1955.

treated as open wounds. Wounds which had partially separated were packed lightly with gauze and allowed to granulate. Antibiotics did not appear to influence the incidence of complications.

In 68 open operations there were no infections and 2 recurrences (2.9%). In 137 closed operations there were 26 (18.8%) separations, 19 (13.9%) infections and 9 (6.6%) recurrences. Differences in choice of procedure and in results were exhibited by the 20 surgeons who performed the operations. One closed 90.9% of the wounds, with 70% complications, another closed 81%, with 11.8% complications and a third closed all wounds, with 60% complications. Since there is every evidence that each surgeon's series was comparable to the others', results seem to depend on the surgeon's choice of operation and his ability to execute it properly.

Average hospitalization following closed operations was 15.3 days compared with 21.0 days following open operations. Since many surgeons prefer to treat patients with open wounds on an ambulatory office basis, length of hospital stay cannot be used as an argument for or against use of either procedure.

Although complications exclusive of recurrence are more numerous in the closed group there is no evidence that this prolonged the time required for wound healing. Average healing time for open wounds was 62.9 days and for sutured wounds packed open because of infection 63 days. Sutured wounds complicated by separation required an average of 33 days to heal completely. Therefore infection and separation are not serious complications if handled properly and likelihood of their occurrence should not prevent the surgeon from closing wounds. Although incidence of recurrence in this series is slightly higher in the closed than in the open group both are acceptably low and the difference is of doubtful significance. It is probably true that the precision with which treatment is carried out is more important than the method.

## HERNIA

**Esophageal Hiatal Hernia Prevalence, Diagnosis and Treatment in American City of 30,000** Jack E Mobley and Norman A Christensen<sup>7</sup> (Mayo Clinic and Found) found 153 esophageal hiatal hernias in adults, aged 29-83, in Rochester, Minn., from Jan 1, 1940 to Jan 1, 1953. Most patients were over 40, and 60% were women. As the prevalence ratio is 5/1000, and incidence ratio 0.5/0.8/1000, it can be predicted that there are well over 800,000 persons in the United States with esophageal hiatal hernia.

Symptoms were present in 121 patients, lower substernal or high epigastric pain or distress being the most frequent. Distress was more noticeable after eating. Stooping or bending frequently induced or aggravated symptoms. Thoracic pain suggestive of coronary insufficiency was present in 16. Dysphagia, usually in the lower substernal region, was the second most common symptom. Hematemesis was present in 10, melena in 7. No symptoms were noted in 20.9%. Obesity was found in 39.6%.

Diagnosis was established by x-ray in 81%, by esophagoscopy in 6% and was made incidentally during the course of an unrelated abdominal operation in 13%. Esophagoscopy is indicated if two x-ray examinations fail to reveal diagnosis, if persistent or intractable pain or dysphagia or both are present—especially when these symptoms fail to subside promptly after medical treatment—if surgical repair is contemplated, if other organic disease processes of the esophagus are suspected, if erosive or ulcerative esophagitis is suspected and if anemia or hemorrhage in upper part of gastrointestinal tract occurs in a patient with esophageal hiatal hernia.

Esophageal hiatal hernias are classified as (1) those without shortening of the esophagus, either with (Fig 127) or without (Fig 128) displacement of the esophagogastric junction and (2) those with shortening of the esophagus, which may be acquired (Fig 129) or congenital. Associated disease may be present. Cholecystitis was found in 24.8%, duodenal ulcer (two gastric) in 23.5%, diverticulosis in

(7) *Gastroenterology* 30:111 January 1956

13.1% and gastrointestinal carcinoma or coronary heart disease in 2.6% each

Conservative medical management was used in 97.4%

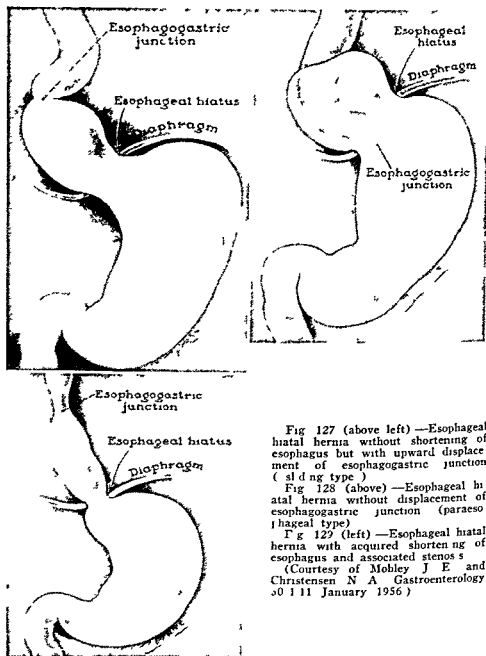


Fig 127 (above left) —Esophageal hiatal hernia without shortening of esophagus but with upward displacement of esophagogastric junction (sliding type)

Fig 128 (above) —Esophageal hiatal hernia without displacement of esophagogastric junction (paraesophageal type)

Fig 129 (left) —Esophageal hiatal hernia with acquired shortening of esophagus and associated stenosis

(Courtesy of Mobley J E and Christensen N A Gastroenterology 30:111 January 1956)

Of 99 patients followed 1-13 years 65% were asymptomatic, and the others had recurrent symptoms, particularly when they were careless about treatment. Patients with gastric hyperacidity are more difficult to treat. As complications are

more frequent in this group, surgical intervention is required more often. The hernias were unchanged roentgenologically or esophagoscopically in 64% of 41 medically treated patients followed for 1-13 years.

Medical treatment includes bland or ulcer diet, with abstinence from alcohol, coffee and tobacco, weight reduction if necessary, elevation of head of the bed 8-12 in., avoidance of tight or constricting garments, mild sedation and antispasmodic agents before meals and at bedtime, antacids an hour after meals and at bedtime and esophageal dilatation, if indicated, to relieve significant localized narrowing.

Surgery was performed in four patients. Surgical treatment is indicated for intractable distress or pain, especially if progressive shortening of the esophagus is present after adequate medical treatment, uncontrollable or repeated hemorrhages with anemia, stenosis not amenable to dilatation and medical management, neoplastic disease involving the hiatal hernia or lower part of the esophagus and amenable to surgery, strangulation of the hernia and perforation of an ulcer in the hiatal hernia sufficient to warrant surgical treatment.

► [Many years ago, patients with inguinal hernia were treated in a manner not very different from that recommended here for esophageal, hiatal hernia. Surgery was used only when the hernia had become very large or was threatened with strangulation. Who would carry out such recommendations now? Similarly, why should anybody wait for such complications to occur as those mentioned in the last paragraph of the abstract. In this modern age the repair of a hiatal hernia is not accompanied by appreciable risk and is not particularly difficult if the operation is carried out before the complications that the authors regard as indications for operation have occurred—Ed.]

**Symptoms of Hiatus Hernia** were analyzed by H. M. Leather<sup>8</sup> (Bristol Royal Infirmary) in 54 of 70 cases in which it was the only detectable lesion. The 33 women and 21 men were aged 21-86, with 40 patients over 50. Sliding hernias were present in 46, paraesophageal, in 6. Two had paraesophageal hernias with regurgitation into the esophagus. Pain, present in 32 (59%), was situated in the epigastrium in 28 and bore no relation to meals in 17. In the others, it occurred within two hours after meals and fatty food was almost always an aggravating factor. Heartburn, noted in 40 (74%), frequently preceded other symptoms by many years. Acid regurgitation was prominent in 36 (67%), 6 of

(8) Brit. M. J. 2:914-937, Oct. 15, 1955.



whom had no preceding heartburn Flatulence, usually post prandial, was present in 38 (70%)

Vomiting was present in 31 (57%) Eight had nocturnal vomiting, often of fairly large quantities, and in most of them this was the presenting and most distressing symptom, often there was no warning nausea Three woke with nausea if they lay on the right side, but sitting up or turning on the left side relieved it and prevented vomiting Relation of symptoms to posture was well marked in 42 (78%) Dysphagia was present in nine (17%)

Appetite was almost always good, 18 were gaining weight, and 16 men and 18 women were obese Five had a history of internal hemorrhage, and three others had intermittently blood streaked mucus Another five had had anemia, sometimes recurrent, which had responded to iron In two, onset of epigastric pain was associated with trauma None of the patients had pain which could be confused with that of myocardial ischemia

However, seven patients (second series), who had been referred to a cardiologist for presumed cardiac pain were later shown to have hiatus hernia In one, pain and 'wind in the chest' on walking, relieved by stopping to belch, was suggestive of cardiac effort pain, but exertion necessary to provoke an attack varied considerably In three, pain in the chest, in the chest and left arm and at the xiphisternum, respectively, could have been mistaken for pain of myocardial ischemia if the patient had been seen only during the first attack In another patient genuine cardiac effort pain was related to anemia and disappeared after iron therapy

In the rare instances in which hiatus hernia is responsible for pain, similar to that of cardiac ischemia, in or spreading to the chest arms neck and jaw direct relation to exertion is inconstant and the pain often lasts for hours Predominant aggravating factors are eating horizontal position and anxiety Relief with belladonna and antacids is usually better than with nitroglycerin

**Pneumoperitoneum in Management of Giant Hernia** is a common procedure in most South American surgical centers, but only two reports of it have appeared in the United States literature One (1947) was by Moreno who originated the method in 1940 the other by Koontz and Graves

(1954) Edward E. Mason<sup>9</sup> (State Univ. of Iowa) reports an initial experience with nine cases and attempts to dispel doubts regarding the value of the method when properly indicated and used.

**TECHNIC**—Local anesthesia is used, and air is injected through a blunt needle into the free peritoneal cavity. A 50 cc syringe with a three way stopcock is attached to the needle by sterile rubber tubing to prevent transmission of motion to the needle during injection. Subsequent refills have been given in amounts and at intervals necessary to keep the patient mildly uncomfortable. An arbitrary total time of one month has been used in most cases. After the initial injection, there is slight shoulder pain for a few days which may be relieved by recumbency. If rapid distention with air is done initially, upper abdominal pain results, probably due to stretching of the liver attachments to the diaphragm. Abdominal pains may sometimes offer a problem in differential diagnosis, but no complication occurred in the present series. Removal of air was not necessary, but this could be used to differentiate stretch pains from signs of complicating intra-abdominal disease. After acute symptoms from pneumoperitoneum subsided, the patients were followed as outpatients, refills were performed as needed, until time for the repair. After the first few days, most patients return to normal activity.

Crossed and overlapped strips of adhesive tape are used to compress the hernia to force air intra-abdominally. The skin is protected with tincture of benzoin, and tapes are extended well out onto the lower chest, flank and thigh. A corset may be used instead of, or in addition to, tape. At the time of refill dressings are tightened. For some extremely large hernias refills may be less frequent and increased intra-abdominal tension can be obtained by increasing the tightness of the tape dressing or corset. Usually the interval between refills is five to seven days.

Emergencies that arise as complications of giant hernias can be treated with that minimum of surgery necessary for the emergency, and subsequent pneumoperitoneum can then be used as required to re-establish the abdominal domain in preparation for definitive and elective repair. Pneumoperitoneum is not a substitute for weight reduction when the latter is indicated, nor does it make unnecessary correction of other adverse influences. It should be used with staged repair if there is inadequate room and/or inadequate abdominal wall for complete repair at the time of the initial operation. When tissues are poor, reinforcement with fascia, tantalum mesh or other appropriate material is not obviated by prior use of pneumoperitoneum.

(9) Surgery 39:143-151, January, 1956

## THE ADRENAL GLANDS

**Bilateral Adrenalectomy in Treatment of Cancer of Breast** Both the ovaries and the adrenals can secrete estrogens that can sustain the growth of mammary cancer. According to Thomas L-Y. Dao and Charles Huggins<sup>1</sup> (Univ. of Chicago), simultaneous bilateral adrenalectomy in a one-stage operation is a practical therapeutic device for selected cases of advanced mammary cancer and provides profound and prolonged relief in a small percentage of patients. The preoperative management includes the correction of any nutritional and electrolyte deficiencies and the administration of large amounts of cortisone acetate the day preceding and during the day of surgery. Postoperatively, desoxycorticosterone acetate is given until the blood pressure is stabilized and the amount of administered cortisone is gradually decreased. Excessive hydration is avoided postoperatively. Severe hypotension is controlled by nor-epinephrine or blood transfusions if hemorrhage is present. The criterion for the adequate hormonal substitution of the adrenalectomized patient is the prevention of any sign or symptom of adrenal insufficiency. Early signs are malaise, anorexia and loss of a sense of well being. Daily oral doses of 37.5-50 mg. cortisone acetate and 1-3 Gm. sodium chloride are usually necessary.

Bilateral adrenalectomy was performed in 173 women and 2 men with far advanced mammary cancer; all had distant metastases. The initial mortality (death within 30 days of operation) was 5% in the first 100 cases; in the rest (75 cases) there was only one postoperative mortality. Of 34 patients who had adrenalectomy alone, 41% had objective remissions; and of 61 patients who had adrenalectomy plus oophorectomy, 41% had objective remissions. Objective remission included regression or disappearance of obvious and easily accessible lesions, such as cutaneous and subcutaneous tumors (Figs 130 and 131) and intra-abdominal masses and also x-ray evidence of calcification of osteolytic lesions and healing of fractures (Figs 132 and 133) and of disappearance of pulmonary lesions and pleural fluid. Many

(1) A M A Arch Surg 71:645-657, November, 1955

of the patients had not responded to earlier treatment with testosterone, estrogens, oophorectomy and irradiation of the ovaries. A profound remission lasting 30 months occurred

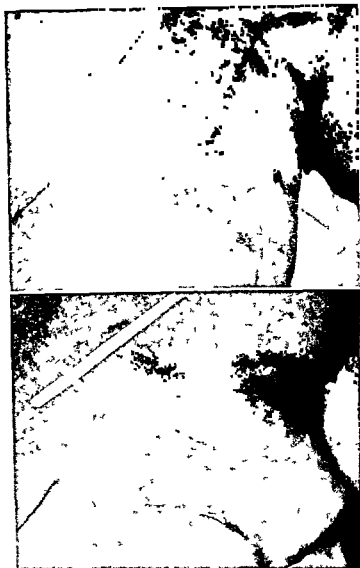


Fig 130 (top) —Extensive local recurrent inflammatory lesion over the mastectomy scar before adrenalectomy

Fig 131 (bottom) —Regression of skin lesion 32 months after operation  
(Courtesy of Dao, T L-Y, and Huggins, C A M A Arch Surg 71 645 657, November, 1955)

in six women, and one woman was alive with marked remission after 49 months.

The mechanism of regression after adrenalectomy is the withdrawal of critical amounts of hormones similar to those found in the ovary. After adrenalectomy in women who have undergone oophorectomy, estrogen is no longer excreted in the urine.

Bone metastases often cause an osteolytic reaction and the elevation of the alkaline phosphatase in serum after therapy. The subsequent decline of the alkaline phosphatase to normal is regarded as indicating increase of osteoblastic activity of bone and healing of metastases. In 24 patients



Fig. 132 (top) —Extensive osteolytic metastatic lesions with multiple pathological fractures in pelvis secondary to mammary cancer before adrenalectomy.

Fig. 133 (bottom) —Healing of pathological fractures and recalcification of osteolytic lesions four years after adrenalectomy.

(Courtesy of Dao T. L. and Huggins C. A. *MA Arch Surg* 71:645-657 November 1955.)

with response following adrenalectomy, the alkaline phosphatase rose to levels higher than the preoperative levels in 20, and there was x-ray evidence of healing of bone metastases. Hypercalciuria and hypercalcemia in advanced mammary cancer indicate rapid bone destruction due to the metastatic disease. In many cases the hypercalcemia and hypercalciuria returned to normal after therapy.

Not all mammary cancer is responsive to adrenal removal. The most responsive tumors are composed of spheroids of microscopic size in which the malignant acini have lumina whose lining is one cell in thickness. The tiny globules contain a secretion which maintains the acini in spheroidal forms. Often the metastatic lesions maintain the original histology of the primary lesion, i.e., with the formation of glands. In 38 cases with a favorable response to adrenalectomy, 73% had adenocarcinoma. Women with high estrogen titer in the urine respond better to adrenalectomy than those who excrete small amounts of estrogen substances.

Androgens and estrogens are not effective in patients who have a relapse following adrenalectomy. Cortisone can effect symptomatic relief in some patients with relapse, but the effects are not profound.

It is not possible to determine accurately before surgery which mammary cancer is hormone dependent. The histologic examination of the primary tumor is not entirely reliable in predicting the response to adrenalectomy.

► [This is an authoritative discussion of the procedure by its originator, Charles Huggins—Ed.]

**Bilateral Adrenalectomy for Advanced Breast Cancer. Report of 11 Cases.** Warner F. Bowers, Theodore H. Nicholas and John J. Kovacic<sup>2</sup> (Brooke Army Hosp., Fort Sam Houston, Tex.) operated only on patients with far advanced cancer who had at least two of the following conditions before adrenalectomy: recurrent skin metastases, roentgenographically demonstrable bone lesions, pleural fluid with demonstrable tumor cells and recurrence or progression after hormone and/or x-ray therapy. Severe bone pain was present in eight patients.

The patients tolerated the surgery well and were kept on 50 mg. cortisone daily by mouth, as maintenance. Of the 11 women, average age 40.8, 8 died 39-620 days after surgery. Pain relief was dramatic and occurred regularly on about the third postoperative day. This relief persisted for variable periods up to one year.

Salt and water metabolism, maintenance of blood pressure, pigmentation and other untoward phenomena were not problems except in two patients who had nausea, vomiting and lowered blood pressure. They required increased

doses of cortisone and had rapid exacerbation of the tumor growth. None of the patients had regression of liver metastases and four died of progressive liver destruction by tumor replacement. All the patients had return of tumor growth after initial inhibition. Adrenalectomy must be regarded as a palliative procedure to be reserved for patients with far advanced disease.

**Clinical Evaluation of Bilateral Adrenalectomy and Oophorectomy for Advanced Mammary Carcinoma** in 50 patients is reported by Maurice Galante and H. J. McCorkle<sup>3</sup> (Univ. of California). Objective evidence of changes in the metastatic lesions were found in 16 patients (36%). *Marked subjective relief of symptoms occurred in 21 and was more pronounced and longer lasting than that obtained with medical adrenalectomy.* Expert management of substitution therapy of adrenalectomized patients is a most essential part of their care.

**Human Adrenal Cortical Autograft into Portal Circulation. Experimental and Clinical Study.** B. Eiseman, R. Hughes, W. Summers and F. Traylor<sup>4</sup> (Denver) report the first successful adrenal autograft in man. During retroperitoneal node dissection and nephrectomy for seminoma the normal right adrenal was cleared of surrounding fat and thin slices of capsule, glomerulosa and margins of fasciculata were implanted into a row of about 20 pockets, 1 cm. in diameter, in the subserosa of the transverse colon and marked with black silk sutures. The left adrenal appeared normal to palpation. No adrenal substitution therapy or ACTH was given postoperatively.

Five months later laparotomy was performed for a benign inflammation. Beneath each silk suture was a small firm, orange yellow nodule of autografted adrenocortical tissue, ranging from 5 mm. to 2 cm. in diameter. Biopsy of two typical areas showed sheets and strands of adrenocortical cells surrounded by a capsule and interlaced with thin fibrous septa. In the subcapsular area, cells typically were well formed, closely packed, darkly staining and appeared similar to normal adrenocortical cells of the zona glomerulosa and zona fasciculata. No evidence of any viable medullary cells was noted.

(3) Am. J. Surg. 90:180-188, August 1955.

(4) Ann. Surg. 142:961-966, December 1955.

The authors' experimental adrenocortical autografts into the portal circulation of totally adrenalectomized dogs resulted in microscopic evidence of successful takes, but surviving cells under conditions employed could not maintain the unsupported animals for a prolonged period. Autografting adrenocortical tissue in dogs by others has usually failed though a few successes have been reported. Rats and rabbits are easily autografted, whereas guinea pigs are more resistant. Survival of a graft depends on adequate vascularity of the recipient bed. Thin slices of grafted endocrine tissue present maximal surface for vascular infiltration and nutrition. The medullary portion of the adrenal does not survive autotransplantation and in the guinea pig, at least, actually impedes successful take of surrounding cortical cells. In rabbits proliferation and growth of autografts occurs only from cells in the subcapsular region of the glomerulosa thus establishing the rationale for using the capsule and underlying subcapsular zona glomerulosa in adrenocortical grafts. Since cortisone replacement is necessary for animal survival following bilateral adrenalectomy, endogenous ACTH secretion is diminished and exogenous ACTH is a necessity in adrenal grafting.

Interest in autotransplantation of adrenocortical tissue into the portal circulation is stimulated by the hope of obviating replacement therapy in patients having palliative adrenalectomy for advanced prostatic and mammary cancer. It is anticipated that trophic androgens from cortical tissue in the portal bed will be inactivated in passage through the liver, while remaining corticoids will be relatively unchanged.

Adrenal Function in the Combat Casualty was studied in 20 critically injured soldiers during the first 7-14 days after injury at a forward surgical hospital in Korea during 1952 by John M. Howard, John M. Olney, John P. Frawley, Ralph E. Peterson and Serfin Guerra.<sup>5</sup> Under the conditions at that time the stress of combat did not lead to adrenal cortex exhaustion. Each casualty showed the adrenal cortex response to trauma. Corticosteroid (formaldehydogenic compounds) excretion rose sharply following trauma. Maximal excretion was sometimes not reached until the 2d day after injury. During an uncomplicated postoperative course,

(5) A M A Arch Surg 71:47-58 July 1955



corticosteroid excretion fell to normal about the 3d or 4th day after injury and then often showed a slight secondary rise. The 24 hour excretion of 17-ketosteroids was usually normal, but in a few patients, slightly elevated. The most marked elevation occurred in a patient who had the most radical debridement, the healthiest wounds and the best hepatic function.

The concentration of circulating eosinophils fell to near zero after injury, but in uncomplicated cases returned to normal a few days later. A rebound increase above normal sometimes followed before concentration stabilized at a normal level. During the first 24 hours after trauma, plasma sodium concentration decreased and potassium concentration rose for a few hours. Retention of sodium and excretion of potassium characteristically resulted in excretion of more potassium than sodium. The ratio of sodium to potassium in urine fell, with injury, to 0.5:0.1. In some patients balance studies showed tremendous and prolonged retention of sodium and loss of potassium.

Repeated traumas resulted in repeated responses of the adrenal cortex. If secondary trauma occurred during primary adrenal response, no further increment could be noted. Subsequently, secondary trauma was characteristically followed by a secondary rise in corticosteroid excretion and in plasma potassium concentration and excretion and by a secondary fall in plasma sodium concentration and often by further sodium conservation. Secondary fall in eosinophile concentration was limited in extent and lasted only a few hours. Wound infection and necrosis were associated with a continued adrenal cortex and electrolytic response of a magnitude and duration not seen in other casualties. The loss of such large quantities of potassium also suggests a process of "metabolic debridement" of necrotic tissue.

**Blood and Urinary Electrolyte Studies in Patients with Hyperfunction of Adrenal Cortex (Cushing's Syndrome)**  
E. Dahl-Iversen, I. Engdahl, E. Hasner, H. Paaby, B. Sørensen and T. Tobiassen<sup>6</sup> (Rigshosp. Copenhagen) determined bicarbonate levels in serum and potassium, sodium and chloride levels in serum and urine daily in 20 women with Cushing's disease. Of the 20 patients, 15 had fairly

(6) *Acta chir. scandinav.* 109:176-180, 1955.

normal electrolytes. In only a few cases did the values indicate hyperfunction of the adrenal cortex.

After subtotal adrenalectomy, 10 patients were studied. All received substitution therapy, either with 5 mg per corten® daily or with 100 mg cortisone twice daily, postoperatively for six days, then the dose was reduced by 50% every third day. No significant difference was noted in the two dosage schedules either clinically or pathophysiologically.

There was no difference between response to general surgery and to subtotal adrenalectomy in Cushing's disease either in time of onset of postoperatively increased excretion of urinary potassium or in duration of increased excretion. No correlation was found between total loss of potassium and postoperative changes in serum potassium concentration. Renal potassium excretion rose between the first and third postoperative days and then fell again, most often below the preoperative levels.

In all cases, serum sodium concentration fell transiently and renal sodium excretion was reduced postoperatively. This reaction occurred later and lasted longer than the potassium response. In Cushing's disease, the reduced urinary sodium excretion occurred later and lasted longer in the postoperative phase than in cases without adrenocortical hyperfunction.

Postoperative serum chloride concentrations were unchanged. No relation was seen among serum chloride and serum bicarbonate concentrations and renal chloride excretion. Postoperative renal chloride excretion was reduced in all cases and coincided with reduced sodium excretion. Early alkalosis seemed more common after resection in Cushing's disease than after general surgery.

Postoperative electrolyte metabolism was identical after subtotal adrenalectomy and after general operations, but chloride sodium retention occurred later and persisted longer in the cases with subtotal adrenalectomy. The protracted retention perhaps was related to per corten® or cortisone administration.

## THE GENITOURINARY SYSTEM

**Observations on Urinary Tract Four to Seven Years after Total Pelvic Exenteration and Wet Colostomy** Alexander Brunschwig and William Daniel<sup>7</sup> (Memorial Center for Cancer, New York) followed 12 patients (from four years to seven years and seven months) who had total pelvic exenteration involving en masse resection of bladder, rectum vagina, pelvic nodes and fatty tissue with implantation of the ureters into the colon with a terminal wet colostomy

Transfer of the ureters to the skin was necessary in one patient because of a persistent bowel and urinary fistula. All patients with wet colostomies returned to full and regular general activities and adjusted well. Slight elevation of the urea or NPN content persisted in four, and there was a slight tendency to hyperchloremia. Carbon dioxide combining power was normal in all but two patients who showed chemical hyperchloremic acidosis. Of 21 individual ureters implanted into the colon, 2 were normal, 6 showed slight dilatation, 10 moderate dilatation with preservation of the calyces' cupping and 3 marked dilatation with obliteration of the calyces' cupping. In no instance did a kidney that was shown to be functioning in a preoperative pyelogram progress to complete nonfunction during the follow up period. Ascending acute pyelitis which occurred twice in one patient was not a problem.

The first postoperative pyelograms after a wet colostomy show some degree of hydronephrosis which usually improves in time. No one pyelogram in itself can reveal the status of the urinary tract after total pelvic exenteration. The urinary tract is capable of adjusting to a transfer of the ureters; there is no evidence of progressive impairment of function with ultimate death.

Anterior pelvic exenteration the same as total pelvic exenteration except that the colon is preserved intact was performed in seven patients followed four to seven years. One patient received cutaneous ureterostomies primarily and six had ureterocolic anastomosis. Severe progressive hydronephrosis occurred in one three developed nonfunc

tioning kidneys (in two due to calculi), four had attacks of pyelitis, three had urinary calculi and in one the ureters were transferred to the skin from the bowel because of progressive hydronephrosis. The patients with anterior pelvic exenteration had more urinary tract difficulty than those with the wet colostomies, probably due to increased pooling of urine and/or retrograde pressure in the colon above the intact anal sphincter.

Formation of a wet colostomy is the method of choice for diversion of both urinary and fecal drainage following total pelvic exenteration. In 181 such operations, there were 35 deaths within one month of surgery (5 due to renal complications) and 10 deaths after one month (2 due to renal complications). Two patients died of uremia less than one year after surgery.

---

## THE EXTREMITIES

**By-pass Operation in Treatment of Arteriosclerotic Occlusive Disease of Lower Extremities** E. Stanley Crawford and Michael E. De Bakey<sup>8</sup> (Baylor Univ.) state that the occlusive process in chronic arteriosclerotic arterial insufficiency of the lower extremities is often segmental, with a patent vessel above and below, and that normal circulation can be restored to the peripheral arterial bed by thromboendarterectomy, excision of the occluded segment and replacement with a graft or by-pass of the diseased area with a graft. *The best method is the by pass operation, which consists in adding a large collateral vessel around the blocked area to the collateral vessels already present, but without disturbing them.* The procedure is based on the natural response of the arterial tree to an occlusive process, namely, the enlargement of collateral vessels around the obstruction. It permits restoration of a normal pulsatile blood flow into the peripheral arterial bed with minimal jeopardy to existing circulatory and functional capacity of the extremity. The minimal dissection required reduces the risk of injury and thrombosis to the main artery and its collateral vessels in the region of occlusion as well as above and below this process. Because adjacent structures such as

(8) Surg. Gynec. & Obst. 101:529-535, November, 1955.

## THE GENITOURINARY SYSTEM

**Observations on Urinary Tract Four to Seven Years after Total Pelvic Exenteration and Wet Colostomy.** Alexander Brunschwig and William Daniel<sup>7</sup> (Memorial Center for Cancer, New York) followed 12 patients (from four years to seven years and seven months) who had total pelvic exenteration involving en masse resection of bladder, rectum, vagina, pelvic nodes and fatty tissue with implantation of the ureters into the colon with a terminal wet colostomy

Transfer of the ureters to the skin was necessary in one patient because of a persistent bowel and urinary fistula. All patients with wet colostomies returned to full and regular general activities and adjusted well. Slight elevation of the urea or NPN content persisted in four, and there was a slight tendency to hyperchloremia. Carbon dioxide combining power was normal in all but two patients, who showed chemical hyperchloremic acidosis. Of 21 individual ureters implanted into the colon, 2 were normal, 6 showed slight dilatation, 10 moderate dilatation with preservation of the calyces' cupping, and 3 marked dilatation with obliteration of the calyces' cupping. In no instance did a kidney that was shown to be functioning in a preoperative pyelogram progress to complete nonfunction during the follow-up period. Ascending acute pyelitis, which occurred twice in one patient, was not a problem.

The first postoperative pyelograms after a wet colostomy show some degree of hydronephrosis which usually improves in time. No one pyelogram in itself can reveal the status of the urinary tract after total pelvic exenteration. The urinary tract is capable of adjusting to a transfer of the ureters, there is no evidence of progressive impairment of function with ultimate death.

Anterior pelvic exenteration, the same as total pelvic exenteration except that the colon is preserved intact, was performed in seven patients followed four to seven years. One patient received cutaneous ureterostomies primarily and six had ureterocolic anastomosis. Severe progressive hydronephrosis occurred in one, three developed nonfunc-

(7) Ann Surg 142:729-738, October, 1955

tioning kidneys (in two due to calculi), four had attacks of pyelitis, three had urinary calculi and in one the ureters were transferred to the skin from the bowel because of progressive hydronephrosis. The patients with anterior pelvic exenteration had more urinary tract difficulty than those with the wet colostomies, probably due to increased pooling of urine and/or retrograde pressure in the colon above the intact anal sphincter.

Formation of a wet colostomy is the method of choice for diversion of both urinary and fecal drainage following total pelvic exenteration. In 181 such operations, there were 35 deaths within one month of surgery (5 due to renal complications) and 10 deaths after one month (2 due to renal complications). Two patients died of uremia less than one year after surgery.

---

## THE EXTREMITIES

**By-pass Operation in Treatment of Arteriosclerotic Occlusive Disease of Lower Extremities** E Stanley Crawford and Michael E. De Bakey<sup>8</sup> (Baylor Univ.) state that the occlusive process in chronic arteriosclerotic arterial insufficiency of the lower extremities is often segmental, with a patent vessel above and below, and that normal circulation can be restored to the peripheral arterial bed by thromboendarterectomy, excision of the occluded segment and replacement with a graft or by pass of the diseased area with a graft. The best method is the by pass operation, which consists in adding a large collateral vessel around the blocked area to the collateral vessels already present, but without disturbing them. The procedure is based on the natural response of the arterial tree to an occlusive process, namely, the enlargement of collateral vessels around the obstruction. It permits restoration of a normal pulsatile blood flow into the peripheral arterial bed with minimal jeopardy to existing circulatory and functional capacity of the extremity. The minimal dissection required reduces the risk of injury and thrombosis to the main artery and its collateral vessels in the region of occlusion as well as above and below this process. Because adjacent structures such

---

(8) Surg. Gynec. & Obst. 101:529-535

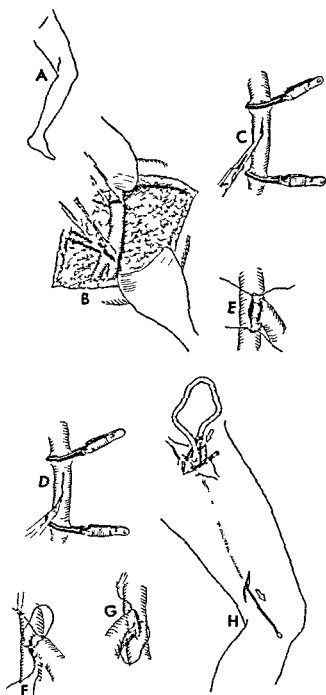


Fig. 134 —Technic of performing by pass procedure for occlusion of superficial femoral artery. (Courtesy of Crawford, E. S., and De Bakey, M. E. Surg., Gynec & Obst. 101: 529-535, November, 1935.)

veins, lymphatics and nerves are not disturbed, complications such as edema, neuralgia and wound infection are largely prevented.

The procedure is accomplished by anastomosis of an arterial homograft end-to-side to the patient's artery above





were observed with gangrene after intravenous therapy administered through a cutdown. A cutdown is used to embrace venipuncture, incision over the vein, venesuture and insertion of a cannula for intravenous therapy, usually required for children when major surgery is scheduled or in the presence of pneumonia, diarrhea and septic and cachectic conditions. Two of the patients had been born prematurely.



Fig. 135 (left) —Gangrene in arm of premature infant after accidental insertion of cannula into left brachial artery.

Fig. 136 (right) —Gangrene of right foot and ankle. Cutdown done in region of medial malleolus.

(Courtesy of Miller, D. S. and Sebeck, R. *Am. J. Dis. Child.* 90:153, 158, August 1955.)

A review of 96 similar cases in the literature revealed one common factor, namely, age. This complication has been most commonly described in young, usually neonatal infants, often of premature birth. One explanation of gangrene, at least in premature and newborn infants, lies in this time of onset, when normal circulatory readjustments are at best demanding.

In this series three patients had general sepsis, one congenital syphilis and one congenital transposition of heart vessels.

Particular care should be given to those infants with severe general sepsis, cachexia and poor tissue nutrition. Lowered resistance in infections is one cause of poor vasomotor response in infants and contributes to ultimate local tissue death even when the outcome is not fatal. Every aseptic safeguard should be used to prevent local infection. Careful handling of tissues for venipuncture is necessary, and especially for incision over a vein, which is imperative to prevent infection and accidental severance of an artery. The vessels should be exposed meticulously, with gentle introduction of the needle or polyethylene tube. Before intravenous therapy is instituted, one should weigh the status of the cardiovascular system and proceed cautiously in the face of any observable signs or deducible implications of circulatory disturbance or inadequacy.

The entity is well illustrated by the following cases.

CASE 1—Boy born at six month term, was started on intravenous therapy one week after birth. A cannula was inserted in the region of the elbow. Three days later the left forearm became cold and cyanotic. The next day the fingers were deeply discolored. The cannula was removed and was found to have entered the left brachial artery on insertion. Procaine hydrochloride, 5 cc of 1% solution, was injected into the left stellate ganglion and hot wet dressings were applied to the arm daily. By the 11th day after birth, moist gangrene, later becoming dry, appeared. The infant died two days later (Fig 135).

CASE 4—Girl aged 6 months hospitalized because of diarrhea and dehydration was given intravenous therapy. A cutdown was made in the region of the medial malleolus of the right leg and a polyethylene tube inserted. Six days later the foot and ankle became cold and blue and pulses were not palpable. The leg and thigh were swollen. Several abrasions preceded gangrene (Fig 136). The child died two days later.

► [This dreadful complication should be avoided at all costs. In infants the placing of a catheter in a vein is not easy. It should be regarded as a major operative procedure. Instead it is often entrusted to inexperienced and uninstructed interns.—Ed.]

**Surgical Lesions of Diabetic Feet** were studied, from standpoints of frequency and cost, both financial and in terms of future disability, in 502 patients (292 females) in 9 hospitals by the Committee on Diabetes, Massachusetts Medical Society<sup>1</sup> (Boston). Although 3 patients were under 20 and 18 under 40, 299 were between 60 and 79 and 22 between 80 and 90 years. Existence of diabetes was not suspected in 42 (8%) before foot lesions appeared, or duration

(1) New England J Med 253:685-688 Oct 20 1955

was estimated at less than six months. In 89, diabetes had existed 6 months to 5 years, 190 had had the disease 5-14 years and 153, 15-30 years.

Absence of dorsalis pedis pulsations was noted in 225, with absence of popliteal pulsation less common and absent femoral pulsation in relatively few gravely ill patients with gangrene. Diagnosis was based on history of intermittent claudication, with the characteristic cold foot, cyanotic when dependent and becoming cadaveric when raised to an angle of 45 degrees, with venous filling delayed beyond 20 seconds. Patients with neuropathy almost always had open areas of infection on toes or over a joint, occasionally with osteomyelitis, characteristically with adequate pulsations or at least good collateral circulation, so that impaired blood supply was not a major factor. These patients manifested lack of pain and had usually walked on an open lesion with local dressings for weeks or months. Knee reflexes were often absent. In patients classified as having primarily infection, the most characteristic lesion was infection in a corn or callus, which often extended into bone or joint because of long neglect. There were also patients who had sustained slight trauma from heat, accidents, pressure or chemical burns followed by infection. In these patients circulation was good. Classification was not certain in 98, of the remaining 404, 48% had arterial insufficiency, with gangrene in 187 cases, 200 had infection in addition to arterial insufficiency, and a similar group had neuropathy.

Among 332 operations, 33 patients (66%) died, giving a surgical mortality of 10%. Causes of death were coronary occlusion in five, pulmonary embolism in six, congestive heart failure in six, atrial and fibrillation in one, cerebrovascular accident in two, infection and toxemia in three, renal failure and uremia in three, and no cause was specified in 7.

Lesions were limited to the toes in 187. Toes, forefoot, sole or heel were involved in 174, and the legs in 127, 13 were not classified as to location. In about a third (170 patients) no amputation or surgical procedure was necessary. In 81, amputations above the ankle were done. The others consisted of amputation of toes with or without incisions for drainage of infection in the feet. Sympathectomies were performed in 20.

The average hospital stay was 26.6 days. It averaged only 14.2 days for patients who required no operation and 33.9 for those with operations above the ankle. The average hospital stay was reduced by numerous deaths during the first few days after operation. Ninety patients were hospitalized 60-100 days. Although the average period of treatment before hospitalization was only 24 days, many patients had had a lesion for a month or two.

Insulin was used on admission by 391 patients, 85 were taking 4-15 units, 214 took 16-40 units, 90, 42-94 units and 4, 100-120 units daily. Although nearly 80% of patients had been taking insulin, use had been intermittent and without adequate medical supervision, and diabetes was not effectively controlled. At discharge, only 42 patients did not require insulin. Freedom from glycosuria without insulin may indicate that diabetes is mild but may not guarantee normal resistance to infection or freedom from progressive occlusive vascular disease. Overeating and excessive weight were predominant features in the history of diabetics with foot lesions.

With an allowance for a period of incapacity before hospital admission and after discharge, cost for these 500 patients can be estimated at \$500,000 without allowance for professional services by physicians or surgeons.

Earlier diagnosis of diabetes and earlier instruction of elderly diabetic patients in care of the feet is urgently needed. That 50% of patients had already had such severe peripheral arteriosclerosis that dorsalis pedis pulsations were absent indicates that their present serious condition will be followed by hospital stays in the next few years. The complete ignorance of many diabetic patients as to the importance of frequent medical check ups and early care of mild lesions of the feet remains a problem and calls for a concerted effort by physicians and community agencies to reach the diabetic public with information that they will use.

Treatment of foot lesions on an ambulatory basis was continued too long in this group. Unwarranted faith in antibiotics or antiseptics in the face of seriously deficient blood supply is a serious hazard. This type of management should be discontinued in active or extending infection, ulcerations on weight bearing points, ulcerations over joints, or that may extend into joints, infected corns or calluses that are

was estimated at less than six months. In 89, diabetes had existed 6 months to 5 years, 190 had had the disease 5-14 years and 153, 15-30 years.

Absence of dorsalis pedis pulsations was noted in 225 with absence of popliteal pulsation less common and absent femoral pulsation in relatively few gravely ill patients with gangrene. Diagnosis was based on history of intermittent claudication, with the characteristic cold foot, cyanotic when dependent and becoming cadaveric when raised to an angle of 45 degrees, with venous filling delayed beyond 20 seconds. Patients with neuropathy almost always had open areas of infection on toes or over a joint, occasionally with osteomyelitis, characteristically with adequate pulsations or at least good collateral circulation, so that impaired blood supply was not a major factor. These patients manifested lack of pain and had usually walked on an open lesion with local dressings for weeks or months. Knee reflexes were often absent. In patients classified as having primarily infection, the most characteristic lesion was infection in a corn or callus, which often extended into bone or joint because of long neglect. There were also patients who had sustained slight trauma from heat, accidents, pressure or chemical burns followed by infection. In these patients circulation was good. Classification was not certain in 98, of the remaining 404, 48% had arterial insufficiency, with gangrene in 187 cases, 200 had infection in addition to arterial insufficiency, and a similar group had neuropathy.

Among 332 operations, 33 patients (6.6%) died, giving a surgical mortality of 10%. Causes of death were coronary occlusion in five, pulmonary embolism in six, congestive heart failure in six, atrial and fibrillation in one, cerebrovascular accident in two, infection and toxemia in three, renal failure and uremia in three, and no cause was specified in 7.

Lesions were limited to the toes in 187. Toes, forefoot, sole or heel were involved in 174, and the legs in 127, 13 were not classified as to location. In about a third (170 patients) no amputation or surgical procedure was necessary. In 81, amputations above the ankle were done. The others consisted of amputation of toes with or without incisions for drainage of infection in the feet. Sympathectomies were performed in 20.

The average hospital stay was 26.6 days. It averaged only 14.2 days for patients who required no operation and 33.9 for those with operations above the ankle. The average hospital stay was reduced by numerous deaths during the first few days after operation. Ninety patients were hospitalized 60-100 days. Although the average period of treatment before hospitalization was only 24 days, many patients had had a lesion for a month or two.

Insulin was used on admission by 391 patients, 85 were taking 4-15 units, 214 took 16-40 units, 90, 42-94 units and 4, 100-120 units daily. Although nearly 80% of patients had been taking insulin, use had been intermittent and without adequate medical supervision and diabetes was not effectively controlled. At discharge only 42 patients did not require insulin. Freedom from glycosuria without insulin may indicate that diabetes is mild but may not guarantee normal resistance to infection or freedom from progressive occlusive vascular disease. Overeating and excessive weight were predominant features in the history of diabetics with foot lesions.

With an allowance for a period of incapacity before hospital admission and after discharge, cost for these 500 patients can be estimated at \$500,000 without allowance for professional services by physicians or surgeons.

Earlier diagnosis of diabetes and earlier instruction of elderly diabetic patients in care of the feet is urgently needed. That 50% of patients had already had such severe peripheral arteriosclerosis that dorsalis pedis pulsations were absent indicates that their present serious condition will be followed by hospital stays in the next few years. The complete ignorance of many diabetic patients as to the importance of frequent medical check ups and early care of mild lesions of the feet remains a problem and calls for a concerted effort by physicians and community agencies to reach the diabetic public with information that they will use.

Treatment of foot lesions on an ambulatory basis was continued too long in this group. Unwarranted faith in antibiotics or antiseptics in the face of seriously deficient blood supply is a serious hazard. This type of management should be discontinued in active or extending infection, ulcerations on weight bearing points, ulcerations over joints, or that may extend into joints, infected corns or calluses that are

deep, and any infection in a foot with arteriosclerotic deficiency of blood supply

Therapy for the Frozen Patient is discussed by A La pras,<sup>2</sup> on the basis of his experiences as physician to the Himalaya expedition in 1955. Frozen extremities are rare in current medical practice, but every physician may have to cope with the acute problems they present. Treatment during the first hours is crucial, and, as Leriche has emphasized, frozen extremities constitute a vascular emergency comparable to arterial embolism. Somewhat contradictory opinions regarding treatment have been upheld, but certain precise directives emerge from the facts.

Prevention is probably the most radical treatment, and is largely a question of equipment, training and organization, which goes beyond the medical aspects of the problem. However, two factors in prevention of freezing at high altitude which should be emphasized are oxygen therapy and hydration. At equal degrees of cold, a subject at 8000 m height may freeze, whereas one at 1,000 m will not. Preventive oxygen therapy, re-establishing approximately normal conditions, diminishes hypoxia, limits polyglobulism and hemoconcentration and prevents tissue anoxia, characteristics of altitude crises which favor peripheral thrombosis. Adequate supply of fluid also limits hemoconcentration and maintains circulating volume. Fluid support at high altitudes should be at least 4 L/man/day to compensate for loss of water resulting from polypnea in a dry atmosphere. The physician attending mountain climbers has to insist on this, because at high altitude fatigue makes them object to the effort of melting snow to obtain adequate quantities of water.

In addition to these general preventive measures, some authors have suggested local application of ointment with vasodilator properties such as cobalt oxide, oral vasodilators or capillary protective agents, such as vitamin PP, rutin and nicotinic acid.

In practice one may be confronted with two different situations depending on whether the patient can be transported rapidly to hospital facilities. When the patient with frozen extremities can be hospitalized promptly, controlled hibernation, sympathetic block, anticoagulants or intra-

arterial perfusion can be chosen. Local care and general supportive measures remain the rule. If freezing has lasted over 16 hours, sympathetic block alone may be tried, since anticoagulants would be ineffective. Recent studies, however, suggest that in cases in which thrombosis is in process of organization, anticoagulants may regain their efficacy by combination with phenylbutazone.

When the frozen patient cannot be hospitalized for many days, as is often the case in a difficult evacuation, Laborit's method of controlled hibernation and intra arterial perfusion cannot be applied. Lumbar infiltrations are possible. Heparin can also be used, because a doctor can always make an intravenous infusion and a coagulation time test, with minimum equipment. In the severe shock which the frozen patient experiences, muffled in a sleeping bag on a rescue sled, it is easier to do an intravenous puncture in the arm than a lumbar infiltration or a successful stellate block. Rapid elimination of heparin minimizes dangers of over-dosage, with consequent hemorrhage, and, to counter this risk, the antidote, protamine sulfate, is available.

In unfavorable cases in which all medical parenteral therapy is difficult, therapeutic effort should be centered on warming of the trunk, and if perfusions are impossible, on making the patient drink 3 or 4 L. of fluid. Attention is directed also to cautious warming of the frozen extremities. ► [I think most doctors like myself who have had no experience in this kind of work will be greatly interested in this article. The forcing of fluids is a new idea to me under these conditions.—Ed.]

**Status of Refrigeration for Amputations and for Tissue Preservation** is discussed by Lyman Weeks Crossman<sup>3</sup> (Baytown, Tex.). Shockless amputations under refrigeration anesthesia are desirable for all patients, not merely those considered poor risks. Refrigeration anesthesia is advantageous because it avoids shock, controls intoxications and avoids anesthetic accidents. Preliminary packing of the limb in ice for one to three days controls intoxication of infectious gangrene better than any antibiotic.

**TECHNIC**—After barbiturate administration and use of a tourniquet around the thigh the leg is buried from the toes to near the groin in about 75 lb. finely chopped ice and wrapped in a rubber sheet. Occasionally the tourniquet can be omitted especially in advanced arteriosclerosis. The leg is removed from the ice when the surgeon is ready to operate and the skin is then dried and prepared.

(3) Am J Surg 91:2298, January 1956



as usual. The amputation is performed, and after visible vessels are ligated and the wound is ready for closure, the tourniquet is removed and all bleeding vessels tied. After the wound is closed, it is covered with a few thin pieces of gauze, and ice bags are placed around it for 24-48 hours to control pain and edema. Infection or doubtful tissue vitality may be reasons for continuing the cooling longer.

Refrigeration can also be used for tissue preservation in partial amputation of a digit or limb or to preserve badly damaged tissues which cannot be treated surgically immediately and is an excellent method of treating burns because it can simultaneously inhibit pain, shock, infection and tissue devitalization. Burns are sufficiently superficial to make the treatment applicable to any part of the body, not merely the limbs. The best emergency treatment is to plunge the burned part immediately into ice water or the coldest water obtainable. This reduces the pain and subsequent inflammation or necrosis. The area should be dressed with a single layer of petrolatum gauze, which can be changed daily without pain, and ice or a refrigerating applicator at ice temperature should be used. Duration of hypothermia is measured by severity of the burn, ranging from a few hours for a minor burn to several weeks if needed. The burn should not be scrubbed or debrided. Antibiotics may be used but are not necessary. If salt is not added to ice, the refrigeration can never cause frostbite because the tissues are not frozen and always retain soft consistency. Immersion foot does not occur. The only dangers of refrigeration therapy for burns are sloughs due to pressure and too long continuance of too low temperature. Temperature should be kept as high as possible but as low as necessary.

**Effect of Delayed Warming on Experimental Frostbite.** Robert B. Lewis and Carl G. Hoak<sup>4</sup> (Randolph Air Force Base) studied the effect on incidence and extent of cutaneous gangrene in frostbitten rabbit legs when rapid warming was delayed for various periods. There were 11 separate experiments on male albino rabbits, in 5 rapid warming was delayed for 30 minutes after freezing, in 3 for one hour, in 2 for two hours and in 1 for four hours. The legs were frozen for 30 minutes in ethyl alcohol-dry ice mixture at  $-15$  to  $-18$  C. Rapid warming was accomplished by immersing the legs in warm water at a temperature of  $42$  C. for five to eight minutes. Incidence and extent of

4) U S Armed Forces M. J. 7:172 178, February, 1956.

skin necrosis was studied at the end of six to nine days. The frozen rabbit legs that were thawed in air at room temperature for 30 minutes and then rapidly warmed for 5-8 minutes in warm water had significantly less gangrene than controls similarly frozen but thawed only in air. Benefit was not obtained when the rapid warming was delayed for one to four hours after freezing. The study indicates that damage occurs not only while the parts are frozen but also during the post-thaw period before tissue temperatures reach normal.

It is of practical importance not only to thaw frozen parts rapidly but also to continue the warming until the parts reach normal body temperature, taking care not to overheat the tissues. Rapid warming should be instituted even after cold-injured parts have thawed, because it cannot be known whether the cold intensity or exposure time or both have been sufficiently great to preclude the saving of tissue. Other things being equal, the benefit obtained will vary indirectly with the length of time the tissue is exposed to cold, either in the cooled or frozen state.

**Shoulder-Hand-Finger Syndrome as a Whole.** According to Erik Moberg<sup>5</sup> (Goteborg), the syndrome has two components—the shoulder and the hand-finger—and usually begins with only one of them. The shoulder component may be caused by immobilizing the shoulder joint, e.g., as in fracture, but even keeping the arm alongside the body in bedridden patients may be enough to cause contracture of the shoulder.

The hand-finger component is first manifested by edema, most prominent dorsally over the metacarpophalangeal and proximal interphalangeal joints. The knuckles lose the ordinary outline, and the creases grow less distinct. Later the skin becomes thin, atrophic, indurated and shiny. Edema may be caused by a hand wound or by damage to central or peripheral neurons and paralysis without any direct hand injury. If an elderly person uses one hand less than usual, due to contracture of the shoulder, for instance, it is enough to cause edema.

Naturally, the hand component does not always follow upon contracture and adhesions in the shoulder or the shoulder component upon hand lesions. However, it is re-

(5) Acta chir scandinav 109 284 292 1955

markable how often a trace of the shoulder component can be found even in early stages of the hand-finger component and vice versa, though the first component may still not trouble the patient

The outlook is usually favorable for the shoulder. If the hand component has progressed so far that edema has already been converted to scar tissue and the ligaments have grown much shorter, the outlook is poor, and no treatment can restore the hand to normal.

In early stages, the shoulder contracture and flexion defect in the fingers usually respond well to active exercising. The patient is told to lift both arms at once and to clench and unclench the hands. In advanced stages, obstacles that the patient himself cannot overcome prevent free movement e.g., adhesions in the shoulder and shortened ligaments in the fingers. Each needs its own local treatment. The shoulder contractures must never be loosened under anesthesia. Shortening of the ligaments in the finger joints can be treated by extremely cautious stretching with elastic bands attached to a glove. Manually executed passive manipulation in the finger joints is nearly always dangerous and brisement force still more so. Paralyzed muscles can be temporarily replaced with passive measures e.g., the flexors in the fingers can be replaced by traction with elastic bands. If one arm is paralyzed at the shoulder, the other arm can be used to support it in the lifting exercises. When there is causalgia special measures are needed to relieve hyperalgesia and abnormal reactions in the sympathetic nervous system.

**Surgery of the Rheumatic Hand.** Hand deformities in rheumatoid arthritis are due not only to primary joint changes but also to myositic contractures, resulting in imbalance between long extensors, long flexors and intrinsic muscles. The most usual deformity is flexion of metacarpophalangeal joints by intrinsic contracture, with secondary contracture of all tissues from skin to bone.

In conservative treatment Sterling Bunnell<sup>16</sup> (San Francisco) recommends mild elastic traction to maintain a functioning position before contractures become fixed, reverse knuckle bender and spring cock up splints and muscle exercise to lessen atrophy. Surgery sometimes results in im-



Fig 137 (top) —Before operation

Fig 138 (bottom) —After operation there was improvement in alignment and function of hand

(Courtesy of Bunnell S J Bone & Joint Surg 37 A 759 766 July 1955)

provement of these pitifully crippled hands, but should be used only in "burned out" cases

In some, arthrodesis is indicated for the wrist, for some finger joints and even for both thumb joints. Tension may be relieved by tenotomy of lateral bands or transverse aponeurosis in the finger. Tension of all three sets of muscles may be relieved by shortening the metacarpals, prefer-

ably at their bases. If dislocations of metacarpophalangeal joints cannot be reduced passively, metacarpal heads must be excised and arthroplasties performed. New joints should be pinned in alignment until enough fibrous tissue contracts around them to give some stability. Thumb deformities are helped by shortening the metacarpal at the base. For flexion contracture of the thumb web the web should be cut across from bases of metacarpals behind to those in front, and fascia and fibrotic adductors dissected and removed, then the cleft can be spread open and fixed temporarily with two crossed Kirschner wires through the first two metacarpals. If no musculature is left, a wedge bone block is used to hold the thumb in opposition, and the cleft is covered with a pedicle skin graft from the abdomen.

Correction of ulnar drift can be done as follows. If metacarpals are shortened at their bases, metacarpophalangeal joints can be extended by tenotomy of lateral bands and of the transverse aponeurosis. Each extensor tendon should be lifted free from the dorsal aponeurosis and transferred and sutured into a slit in the dorsal aponeurosis on the radial side of the knuckle. If arthroplasties are done, a similar procedure may be used. Tendon transfer of extensor indicis proprius to the radial side of the lateral band of the index finger and similar transfer for the little finger will furnish adduction to these fingers.

Woman, 45, whose rheumatoid arthritis had been quiescent for 17 years had intrinsic contracture of all digits. Proximal finger joints were irreducibly dislocated and extensor tendons luxated with ulnar deviation of 40 degrees and typical thumb deformity (Fig 137). At operation on the right hand 1 in. of the distal end of the finger metacarpals was excised and the phalanges were temporarily pinned to metacarpal stumps. Extensor proprius tendons were transferred to radial side of index and little fingers. Ulnar drift was corrected and function of hand improved (Fig 138) so that she can extend the fingers fairly well, has a stronger grip, picks up objects better and uses all fingers on the typewriter.

**Suture of Finger Tendons.** According to Walter Dick<sup>7</sup> (Univ. of Tübingen), most surgical textbooks convey the mistaken impression that a severed tendon should always be sutured and that tendon suture is simple and easy. The general practitioner should refer treatment of tendon injuries to a specialist. The surgeon concerned should recognize that a severed tendon per se is not necessarily an indi-

cation for tendon suture. The chief surgeon should remember that suture of a tendon is not an operation for novices. The specialist and teacher of surgery of the hand should take the time and trouble to acquire special knowledge and skill in this field.

Recently it has been recognized that end results of treatment are poor—much poorer than many physicians and even specialists believe. Earlier statistics are misleading because injuries in which tendons were intact were included with severed tendons and no distinction was made between flexor and extensor tendon lesions or between cutting of connected aponeuroses and single tendons. Success or failure of suture depends largely on the location of the severed tendon.

Injuries which do not interrupt tendon continuity cause no functional loss, and to suture such a tendon, as is frequently done, is superfluous and dangerous because introduction of the foreign body (suture) may cause infection or functional impairment. Indicated treatment is cleansing of the wound, immobilization and antibiotics by mouth.

Every open injury in which a tendon is severed leads to functional failure of the involved muscle and carries danger of infection. Prevention of infection is more important than repairing the severed tendon. Suppuration occurs in about 20% of tendons sutured immediately, and antibiotics have not reduced the incidence significantly. Late sutures do not become infected, and any cut tendon that does not lead to functional disability, e.g., palmaris longus, should not be sutured. When interruption of a tendon causes severe loss of function, suturing is attempted, provided location of the lesion gives prospect of success. When prognosis is doubtful, suturing should be postponed, whatever the degree of functional loss. Complete severing of an extensor tendon, especially aponeuroses in the finger and hand, produces loss of active extensibility with considerable disability, since prognosis for healing is favorable, immediate suture is indicated.

When other conditions are unfavorable, attempt to restore tendon continuity is made by late suture after healing of the wound. Early suture of flexor tendons, from the palm of the hand to the terminal joint, is always unsuccessful and must not be attempted even when functional damage

is severe. When only the superficial tendon is cut, it is not sutured. When deep flexor tendons of the finger are cut, ankylosis of finger and joint in a functional position produces a useful finger. With cutting of both flexor tendons, reconstruction of only one is undertaken, perhaps with removal of the other. When both flexor tendons are severed, free tendon transplantation may restore function.

Late tendon suture is considered when treatment of the original injury was delayed or immediate suture was contraindicated, when a severed tendon was overlooked (this should not happen, but sometimes does) or when the physician who first treated the patient was unable to perform tendon suture or had to work under conditions in which asepsis could not be maintained.

Early suture is indicated only when the surgeon can do an atraumatic repair, i.e., with very fine, sharp instruments, finest suture materials, pneumatic evacuation of blood, avoidance of infiltration anesthesia and all local applications of chemicals or antibiotics, no disturbance of the tendon with finger or instrument, avoidance of a dry point, no heat from the operating lamp, avoidance of hematoma, no drainage tubes and careful covering of the suture with soft tissue.

After muscular shrinkage, late suture is often impossible, since tendon ends cannot be approximated. Hence late suture should be undertaken within a month after injury, but unfortunately, quite often wound healing is delayed. Then transplantation must be done instead. Artificial materials have so far not proved successful, because of foreign body reaction of the surrounding tissue. Free autoplasmic tendon transplantation—palmaris or extensor tendon of third or fourth toe—yields results comparable to direct suture. Reconstructive procedures on finger tendons are justified only when the finger has sufficient circulation, adequate soft tissue covering, retention of sensory function (or these can be achieved by preliminary operation) and a freely moveable, but not disconnected joint. Satisfactory results also depend on co-operation of the patient.

**Some Remarks on Repair of Flexor Tendons in the Hand, with Particular Reference to Technic of Free Grafting** are presented by A. B. Watson<sup>8</sup> (Birmingham). Divisions of

the flexor tendons in the palm should be repaired by direct end-to-end suture, with a crisscross stitch of braided stainless steel on nontraumatic needles, followed by immobilization for three weeks. Divisions of the flexor pollicis longus should be repaired within its sheath with direct suture, pro-

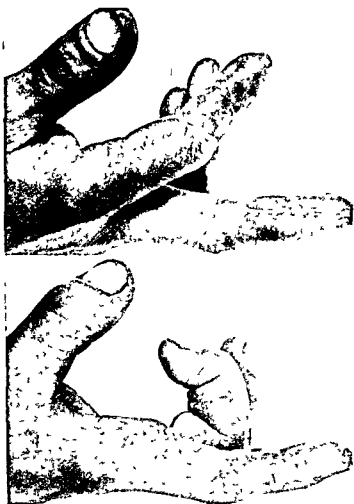


Fig 139 —Perfect results, in man, 36, of repair of profundus tendon in middle finger, cut within  $\frac{1}{2}$  in. of its attachment and reattached by indwelling wire suture (Courtesy of Watson, A B Brit J Surg 43 35 42, July, 1955)

vided the ends have not retracted too far, when a tendon graft is necessary. Division of the profundus only, within  $\frac{1}{2}$  in. of its attachment to the base of the terminal phalanx, can be repaired by a stainless steel wire which holds both sides of the tendon and is taken out through either side of, and tied across the back of, the nail. Some patients regain full use of the finger (Fig. 139), whereas others continue to have a stiff finger.



When both tendons are divided at any point within the digital sheath and when the profundus alone is divided at any point proximal to  $\frac{1}{2}$  in, from its attachment, a free tendon graft should be used. The best donor graft is one of the toe extensor tendons because it is always present, its removal does not upset the foot and it is small, strong and available at sufficient length.

**TECHNIC**—The whole length of the finger is exposed by an incision in the midline of the lateral aspect of the finger. As much of the flexor sheath as possible is preserved but any damaged sheath is excised. A hole is made through the base of the terminal phalanx with an Archimedes drill and a dental bur, and the distal end of the sublimis is excised. An intact sublimis is not removed. The proximal end of the profundus is located and withdrawn into the finger wound and attached to a length of thread. The palm is incised and the proximal ends of the sublimis and profundus located. Only transverse incisions are made in the palm. The elasticity of the muscle belly is determined as its inelasticity leads to poor results. The tendon graft is removed from the fourth toe through an incision along the whole length of the tendon. A branch of the sural nerve below the tendon is preserved. As much paratenon as possible is removed.

A V cut is made in the profundus just distal to the lumbrical attachment and one end of the free graft is placed into this cut and anchored by interrupted braided stainless steel sutures. The free end of the graft is attached to the thread which has been pulled through the tendon sheath tunnel from the finger. The tendon is easily threaded through the remaining tendon sheath tunnels in the finger and through the hole in the base of the terminal phalanx. If portions of the tendon sheath are not sufficient to prevent bowstringing of the tendon, a length of another toe extensor tendon, usually the fifth, can be threaded around the phalanx between the bone and the extensor tendon and around the free graft and tightened sufficiently to keep the tendon in reasonable apposition to the anterior surface of the phalanx. The tendon should be made a trifle too short. The finger should be immobilized in a plaster of paris splint in a neutral position for three weeks. During surgery a tourniquet should be used to prevent bleeding.

Contraindications to tendon repair are sepsis, damage to the digital nerve and absence of passive flexion from the finger. The final results of the operation should not be assessed for at least 12 months and should be good.

**Freeze-Dried Arteries Used as Tendon Sheaths** In tendon surgery, major problems are prevention of adhesions and maintenance of free gliding motion. It is thought that adhesions are initiated by the paratenon and surrounding tissue and not by the tendon itself. Procedures designed to prevent adhesions operate in one of two ways. In one, a

new smooth-walled tunnel is allowed to form around a tubular mold to provide a gliding surface for the tendon after the mold is removed. In the other, the tendon is sheathed during healing with a substance that is less likely to adhere to the tendon than surrounding connective tissue. Of inorganic and organic materials used in the latter procedure only polyethylene was satisfactory, but with it the time required for tendon healing was doubled.

D. R. Koth and W. H. Sewell<sup>9</sup> (Nat'l Naval Med. Center, Bethesda, Md.) tried freeze-dried homologous arterial im-



Fig. 140—Arterial homograft sheath after six months has been split longitudinally and the tendon retracted, note smooth, shiny, gliding surface and absence of adhesions (Courtesy of Koth, D. R., and Sewell, W. H. Surg, Gynec & Obst 101: 615 620, November, 1955)

plants and found that, when they were placed around traumatized tendons as a sleeve, they prevented adhesions between the tendon and the surrounding tissue (Fig. 140). The implant was replaced by fibroblasts, and a new gliding surface was provided for the tendon. Freeze-dried heterologous arterial implants, used in the same manner, were not successful, owing to excessive fibrosis and scarring. In presence of infection, the freeze-dried material was wholly or partially destroyed. This method of preventing adhesions may be useful in the clinical technics of tendon surgery.

**Dorsal Acetabular Fractures of Hip (Dashboard Fractures).** Åke Waller<sup>1</sup> (Univ. of Uppsala) reports 106 cases (89% of patients were aged 21-61), 61% of which were

(9) Surg, Gynec & Obst 101 615 620, November, 1955

(1) Acta chir scandinav, supp 205, 1955

caused by automobile accidents. The frequency of this injury, which usually occurs after a violent impact against the knee or foot, with the hip flexed, has increased since World War II. Combination with other injuries, such as those to the patella and knee, was high. Of the 106 cases, 24 were type I—fracture of posterior superior part of the acetabulum with moderate or no displacement, 43 were type II—fracture with single fragment of posterior-superior part of the acetabulum, with extensive displacement and dislocation of the femoral head, and 39 were type III—comminuted fracture. For x-ray diagnosis, a posterior oblique x ray, as well as the usual frontal and side projections, is needed.

Types II and III are easily diagnosed clinically. If the femoral head is dislocated posteriorly out of the hip joint, the dislocated limb assumes the typical position of adduction, medial rotation and shortening of about 2.5 cm observed by comparing the inner ankles, with the patient lying supine. The knee joint is slightly flexed and the toe often rests on the tarsus of the other foot. The femoral head may be palpated in its dorsal position. Passive movement of the injured hip is painful and abduction is restricted. Crepitus is found. In type I injury, the leg does not assume a characteristic position and the femoral head is not palpable.

Early complications included sciatic nerve injury in 24, myositis ossificans in 14, fracture of the femoral head in 8, thrombosis in 6, urinary tract injuries in 3 and retroperitoneal hemorrhage in 1. Late complications in 87 followed: patients were avascular necrosis of femoral head in 17 and traumatic arthritis in 39. In cases of minor fractures, symptoms of sciatic nerve irritation may be due to stretching of the nerve or pressure from hemorrhage and may be transient, requiring no therapy. In large fractures with a displaced fragment and in comminuted fractures, the sciatic nerve area must be explored and hematomas drained, fragments removed and the hip joint structure restored as much as possible. Early reduction and prevention of redislocation reduce the risks of myositis ossificans. Radiotherapy does not help myositis ossificans.

Of the 87 followed patients, 60 were treated by closed methods and 27 by open methods. Closed treatment proved to be suitable only in the mildest cases with type I fractures; in the other types it gave unsatisfactory results, with

full reduction of displaced fragments in only 2 of 42 cases. In nine cases with initial sciatic nerve injury, five with paresis and four with milder lesions, improvement was obtained only in two mild cases. Incidence of arthritic changes was high in fractures of types II and III. Of the 60 patients, 22 had excellent to good results and 38 fair to poor results.

All 27 patients treated by open methods had fractures of type II or III. Early results were encouraging. Full reduction of displaced fragments was obtained in 21 cases. Among 15 patients with initial nerve injuries, there was complete restitution in 9 of 11 mild cases and improvement in 1 of 4 paralytic cases. Of the remaining three patients with paresis, two had been operated on more than two months after injury. Traumatic arthritis occurred in 10% with type II fractures and in 47% with type III fractures. The period of observation was shorter than with the closed method. Seventeen patients had excellent to good results and 10 fair to poor results.

The study shows that open treatment is best. Closed treatment should be adopted only in the mildest type I fractures. Sciatic nerve symptoms must be looked for and operation performed as early as possible when they are discovered.

**Massive Sliding Inlay Bone Graft for Correction of Ununited Fractures of Long Bones** J. Huber Wagner and Francis P. Ferraro<sup>2</sup> (Pittsburgh) present a type of bone grafting procedure that has been used 207 times on 182 patients in the course of 196 operations in the past 33 years with excellent results.

**TECHNIC**—Using an adequate incision to expose the bone above and below the ununited fracture, any sinus tract is excised. After the bone is exposed, the site of the ununited fracture is completely cleaned out with removal of all fibrous and bony tissue between the bone ends as well as in the surrounding soft tissues. The soft tissue must be free from calcific deposits or dense fibrous tissue. The bone ends are then freed and the rounded off, scarred and closed off portions of the bone involving the ununited fracture are freshened by completely removing the tissues. The marrow cavity is opened above and below the site of the ununited fracture. Bone fragments are aligned and the bone graft is outlined. The grafts are cut in situ with an electric saw. The graft is then removed, reversed and placed in such a position that the larger graft fits into the mortise, traverses the fracture line and extends far enough above this area to insure

good bridging and fixation. The smaller graft is used to fill in the remaining gap in the bone. Internal fixation may have to be used, depending on local circumstances.

The advantages of the method are that a bone bank is not necessary, autogenous bone is much better than heterogenous or even homogenous bone, bone taken from the bone involved in the ununited fracture is better than bone taken from any other part of the body and the medullary canal is opened to insure good healing. The grafts heal by blending into the major bone fragments above and below the traversed fracture site. Bone healing takes place across the multiple fracture sites with little or no subperiosteal callus formation. At the same time, the osteogenetic process set up by the fresh marrow across the site of the ununited fracture stimulates healing and bone formation and brings about the production of enough new bone to bridge the ununited fracture and to blend this in with the bone graft proper. The final result looks more like a bone which had a simple reduction of a fracture with internal fixation.

Complications of the procedure include fracture of the graft across the site of the ununited fracture, fracture of the shaft through the donor site above or below the site of the ununited fracture, and infection.

**Glomus Tumors: Analysis of 25 Cases** According to Charles Horton, Carter Maguire, Nicholas Georgiade and Kenneth Pickrell<sup>3</sup> (Duke Univ.), glomus tumors are not so rare as supposed. The normal glomus is an end organ apparatus consisting of an arteriovenous anastomosis functioning without an intermediary capillary bed. The glomus consists of an afferent artery which is connected directly to a primary collecting vein by a tortuous anastomotic vessel, which is endothelial-lined and surrounded by smooth muscle fibers and glomal cells that are covered by a delicate collagenous material through which run numerous nonmyelinated nerve fibers. The glomic system is found in the stratum reticulare of the skin. Normally, glomic structures are distributed widely over the body, but they are more numerous on the extremities, particularly the fingers and toes. The function of the glomus is thought to be related to the control of the arteriovenous circulation of the skin. The shunt allows the body to regulate the local and

general body temperature by the dissipation or conservation of heat. The glomus is controlled by the autonomic nervous system.

Typically, the glomus tumor is a single tumor, often deep red to purple or blue in color. The tumor is rarely larger than 2-5 mm., and it consists of a slightly raised, bluish, tender subcutaneous nodule (Figs. 141 and 142). The subungual area is a favorite site. Most tumors are very painful and tender to touch. Even slight pressure may cause

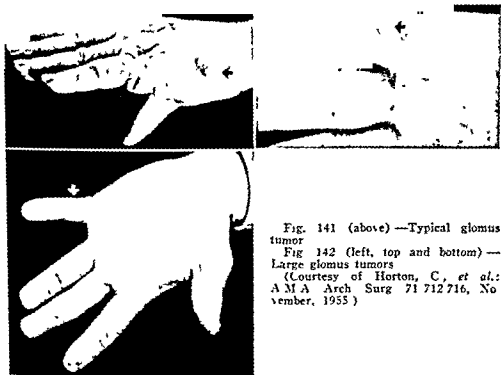


Fig. 141 (above) —Typical glomus tumor

Fig. 142 (left, top and bottom) — Large glomus tumors

(Courtesy of Horton, C., et al.: A M A Arch Surg 71 712 716, November, 1955)

lancinating or radiating pain, which may also occur with temperature changes or changes in position of the lesion. When the lesion is subungual, the nail is often thickened and ridged. Owing to their expansile character, these tumors sometimes erode bone. Although pain is usually severe, a subcutaneous glomus tumor may not be visible. The tumor can be found by pricking the area with a pin. There is no known etiologic factor.

Microscopically, a glomus tumor resembles a normal glomus except for an increase in glomal cells and nonmyelinated nerve fibers. These tumors must be differentiated from neuromas, lipomas, hemangiomas and fibromas. The tumor is benign, and complete removal by surgery is curative. If hemangiopericytoma is diagnosed, a more extensive

local excision is necessary, since invasion and metastasis may occur

The authors report on glomus tumors in 16 women and 9 men, aged 18-70. Most of the tumors were on the extremities. Only one tumor was subungual.

**Benign and Malignant Giant Cell Tumors of Bone: Clinical-Pathologic Evaluation of 31 Cases** is made by William R. Murphy and Lauren V. Ackerman<sup>4</sup> (Washington Univ.) in 13 males and 18 females, aged 14-61. The most common locations of the tumor were the distal end of the femur, in eight, and the proximal end of the tibia, in seven. The average duration of symptoms before diagnosis was nine months. Pain was present in 22 cases and enlargement of the affected bone in 16. Calcium, phosphorus and alkaline phosphatase determinations in 11 were normal. The microscopic diagnosis is often difficult, and the condition must be differentiated from aneurysmal bone cyst, nonosteogenic fibroma, fibrous dysplasia, chondroblastoma, osteitis fibrosa cystica, giant cell tumor of the tendon sheath, osteoid osteoma, osteogenic sarcoma and callus.

There were 26 cases of benign giant cell tumor. Surgery was an effective means of therapy. No series of genuine giant cell tumors treated by irradiation has been reported that adequately shows the effectiveness of irradiation as the only treatment. There is no evidence that well planned radiation therapy causes a benign giant cell tumor to become malignant. Combined surgery and irradiation probably are not warranted as a primary method of treatment and has not been more effective than surgery alone. If the tumor is located in a bone in which excision does not imply loss of adequate function or deformity, then that is the treatment most likely to eradicate the disease. The treatment of choice of lesions in bones that should not be resected and are accessible to curettage is not entirely clear. Curettage is effective whether irradiation is as good as curettage in

in 11 instances, cartilage formation was not seen. Bone and osteoid showed no relation to recurrence but were occasionally confusing in distinguishing osteosarcoma with giant cells from malignant giant cell tumor. Recurrence is also related to adequacy of treatment and to variation in tumor susceptibility to radiation.

There is no doubt that giant cell tumors are true neoplasms and at times may be malignant. Of the 31 cases, 5 were interpreted as being malignant from the histologic appearance and clinical manifestations at the time of first examination or during the subsequent course. Two were considered malignant at first histologic examination. There were two cases of benign giant cell tumor with apparent transformation to fibrosarcoma with metastases and fatal termination. There was one case of histologically benign giant cell tumor with pulmonary metastases having the appearance of benign giant cell tumor, the patient was well more than seven years after a second thoracotomy for removal of metastases.

Diagnosis of malignant giant cell tumors may at times be difficult. Differentiation from osteosarcomas containing large numbers of giant cells is hard. The presence of osteoid and bone cannot be used as an absolute criterion to distinguish the tumors. The presence of cartilage or chondroid is evidence against malignancy. The character of the stroma and giant cells is the best means of determining malignancy, the character of the giant cells is helpful because they usually do not show the same pleomorphism and number of mitoses as the surrounding stroma. However, these cells may be misleading, they may at times show slight pleomorphism and occasional mitosis. The stroma of malignant tumors is composed of quite vascular, loosely arranged cells, with little intercellular material. Malignant giant cells with few pleomorphic nuclei can be seen in addition to benign giant cells with numerous small regular nuclei.

► [It is interesting that when these tumors occur in the long bones they develop at the sites where we used to find acute osteomyelitis, namely, between the epiphysis and diaphysis in the region of the bone designated by Kocher as the metaphysis.—Ed.]

**Interilio-Abdominal Amputation**, ("hindquarter") defined by H. Melega<sup>5</sup> (São Paulo) as total or subtotal removal of a lower extremity, had been reported in 257 cases by 1950.

(5) Lyon chir 50 909 916 Nov Dec 1955



This operation is indicated in several conditions, but malignant tumor is by far the most important (78.61%). A high proportion (45.61%) of patients died the first two years.

Melega's technic differs from that of Assali and Sohler (1937) in the following respects: (1) The abdominal portion of the incision is placed higher, in an effort to avoid incision into Scarpa's triangle, which often is contaminated by metastases. (2) Primary hemostasis is applied to external iliac vessels and not to femoral arteries, to avoid dissections in Scarpa's triangle. (3) All large nerve trunks are sectioned before bone is cut, to avoid traction on large nerves, which would favor shock. (4) Lymph nodes are scooped out at least to the bifurcation of the aorta. Amputation is preferable to disarticulation, when the case permits it. Although excision of the iliac bone has the advantage of being more radical, section presents certain advantages: (1) It is technically easier. (2) It retains insertion of important muscles in maintaining the position of the pelvis and avoiding high deviation of the remaining half. (3) It does not require disinsertion of the corpora cavernosa. (4) It does not sacrifice the obturator muscle.

When the extent of the lesion demands disarticulation, it is less shocking to do sacroiliac articulation and to extirpate remaining fragments of iliac bone later. When the lesion includes one of the two joints, an intermediate operation can be done, such as interpubic disarticulation with section of the iliac wing, or vice versa. The posterior musculocutaneous incision is preferred, with preventive hemostasis by ligation of external iliac vessels. Buttock arteries, branches of the internal iliac, are thus preserved.

Of 10 cases reported, 4 amputations were done for malignant melanoma, 2 for sarcoma, 2 for metastases from cancer of the penis and 2 for "cellular polymorphism." One patient died on the operating table, another from postoperative pulmonary embolism. Five died from cancer: 2, 2½, 5, 10 and 17 months after operation. One patient with osteogenic sarcoma was living and well five years after operation, but was later lost to follow up, and two who had amputations for malignant melanoma were living and well two and four years after operation.

► [One wonders if this mutilation is worth while. Would a large enough series of cases to make the statistics significant show that any patients have really been salvaged?—Ed.]

# ANESTHESIA

Edited by  
STUART C. CULLEN, M.D.

---

## DEPRESSANT DRUGS

**Spirometry in Assessment of Analgesia after Abdominal Surgery** Method of Comparing Analgesic Drugs in patients who have undergone upper abdominal operations is described by P R Bromage<sup>1</sup> A drug that removes pain effectively will also restore vital capacity closer to normal than one which does not relieve pain Comparison of vital capacities after administration of different analgesics provides quantitative indication of amount of pain relief obtained with each (Fig 143) Comparison of vital capacity before and again after operation, when the patient is fully recovered from the anesthetic, indicates the amount of respiratory impairment caused by the pain A perfect analgesic will restore vital capacity to normal, or nearly so, whereas an ineffectual drug will make no difference Amount of restoration of vital capacity expressed as a percentage of impairment caused by pain yields a quantitative basis for comparing different drugs in the same and also in different patients Percentage restoration of vital capacity (VC) can be called the respiratory restoration factor (RRF) of the drug and is a measure of analgesic effectiveness It is calculated by this formula

$$RRF = \frac{\text{analgesic VC} - \text{pain VC}}{\text{preoperative VC} - \text{pain VC}} \times 100$$

Three different types of postoperative analgesia evaluated by comparison of RRF's in 20 patients were (1) regional analgesia by epidural spinal block with an indwelling epidural catheter, (2) systemic analgesia with pethidine and methadone (amidone), (3) systemic analgesia using a local analgesic (lidocaine hydrochloride—xylocaine®) intrave-

(1) Brit M J 2 589 593 Sept 3 1955

## ANESTHESIA

nously. Mean RRF in 17 observations for epidural anesthesia was 80.2; for pethidine (12 tests), 13.5; for amidon (14 tests), 35.4 and for xylocaine® intravenously (9 observations), 22.8.

Results of this method of comparison, based on vou

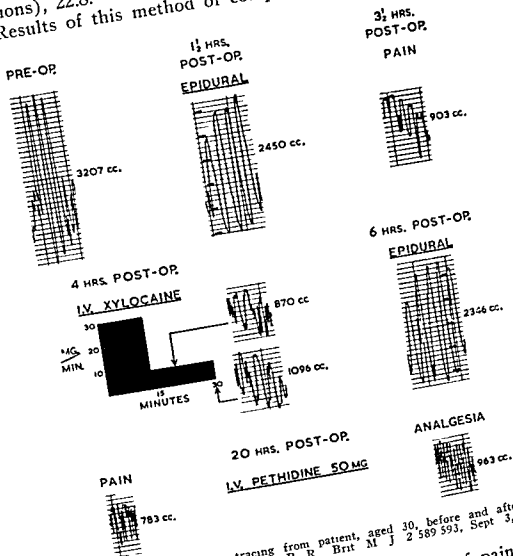


Fig 143—Vital capacity tracing from patient, aged 30, before and after total gastrectomy (Courtesy of Bromage, P R Brit M J 2 589 593, Sept 3, 1955)

pain, may not be applicable to other types of pain. The method is deliberately designed to measure relief of pain in an inherently painful situation, whereas many analgesics act by removing the painful situation and not by dulling the pain. For example, although pethidine scores poorly in this series, it may be valuable in pain from smooth muscle spasm, such as ureteric colic, for relief of this pain is partly due to direct antispasmodic action.

► [The author's assumption that effective analgesics in the treatment of

postoperative pain restore normal ventilation is open to debate on several counts. Impairment of ventilation even in the presence of pain may be due to other factors such as position restrictive bandages, apprehension and so on. In addition unless the dose of analgesic is limited to that required to control pain depression of ventilation may be produced by the narcotic. Indirectly, however, the author points up the need for using these drugs in precise doses, that is, a dose which will provide pain relief without side effects such as depression of respiration or cough reflex. Furthermore, restriction of ventilation due to pain should raise the question of the value of having patients 'wide awake' in the immediate postanesthetic period—Ed.]

**Use of Chlorpromazine in Obstetric Sedation.** Harry I Norton, Maxwell Weingarten and Edward T McDonough<sup>2</sup> (Rochester, N Y) studied 109 patients given chlorpromazine with seconal\* and scopolamine and 109 controls given demerol\* and scopolamine. With chlorpromazine, 68 (62.5%) had complete "amnesia analgesia", 26 (24%), fair results and 15 (13.5%), poor reactions. Objectively, 69 patients (63%) were well controlled, awaking when roused but not with labor contractions, 19 (16%) were slightly active and 21 (21%) were poorly controlled, being very active and requiring constant supervision, among controls, 65% were well controlled, 20% slightly active and 15% poorly controlled. Little difference was noted in the amount of anesthetic agent (usually cyclopropane) required for induction. The impression of the anesthetist was that when difficulties, such as laryngospasm, were encountered, they were not so severe and more easily controlled when chlorpromazine was used.

In the chlorpromazine treated group, three stillbirths occurred, two, before labor. Prompt respiratory response occurred in 92, including 3 premature infants under 2,500 Gm. Six had apnea for over 60 seconds but less than 4 minutes, seven required intubation and resuscitation for 4-10 minutes. Among the controls no stillbirths occurred, and 96 responded well at birth. Four were apneic, requiring pharyngeal suction, and nine required active resuscitation with intubation.

In the treated group two patients had nausea and one vomited at least once before delivery. Among controls, four had nausea, and six vomited before delivery. Incidence of symptoms in treated patients was 27% and in controls 9.1%. Chlorpromazine did not appear to exert any significant effect on length of labor.

(<sup>2</sup>) Am J Obst & Gynec 71:1251-1257 June 1956

No harmful effect was observed on any mother who received chlorpromazine. Chlorpromazine potentiated not only the good effects of drugs used with it but also the undesirable side effects, such as restlessness, excitement, etc. It compared favorably with the control medication and obviously may be useful in patients in whom narcotics are contraindicated.

► [The reduction of nausea and emesis in patients treated with chlorpromazine is significant but this does not differ from the experience with non-obstetric patients. Significance of the influence of chlorpromazine on other factors such as labor, delivery and infants is not convincing. The authors also participate in the common misapplication of the word "potentiation." There is no evidence presented to indicate that anything other than simple addition of effect of drugs was demonstrated.—Ed.]

**Clinical Evaluation of Chlorpromazine in Management of Labor** is presented by Umberto E. Anz and Louis J. Smith<sup>3</sup> (Los Angeles). Initial medication for 20 patients was 25 mg chlorpromazine and 50 mg meperidine, intramuscularly, 35% required a second injection. Analgesia was poor in 10%. Only 15% had amnesia after one or more injections. Of 100 patients treated similarly, except that 0.4 mg scopolamine was added to the initial injection, 33 required a second injection and 1 a third. Medication was satisfactory in 95% and excellent in 49%. Amnesia occurred after the first or second injection in 30%. Effective duration of initial medication varied considerably. Of 40 patients who required supplementary injection (24 primigravidas), 22.5% received it about two hours after, 35% three hours after and 15% four hours after the initial injection, only 27.5% had relief for more than four hours after the first injection.

Resuscitation of infants was required in 24.5% of 135 patients in whom chlorpromazine was used and in 52.9% of 150 cases not treated with chlorpromazine. Not one infant in the chlorpromazine group required active resuscitation.

Only 12.5% of the mothers had drop in systolic pressure over 20 mm Hg after receiving chlorpromazine, and none had shock or required therapy. Among 100 patients who received chlorpromazine and spinal anesthesia, systolic blood pressure fell over 20 mm Hg in five, in four of these, epinephrine intravenously brought prompt response. Three of the five patients were anesthetized within an hour after receiving chlorpromazine.

No untoward local tissue reactions occurred after chlorpromazine. Only one patient had moderate pain at the injection site. Diluting chlorpromazine with meperidine and scopolamine apparently results in a less irritating solution. ► [The reduction in necessity for resuscitation of infants delivered of mothers receiving chlorpromazine is significant. However, as in many clinical investigations, the drugs were not administered as unknowns and the resulting handling of patients, infants and observations is subject to conscious or unconscious bias.—Ed.]

**Perinatal Hypoxia Caused by Obstetric Analgesia and Its Avoidance by Use of Prodine.** According to Arthur G. King<sup>4</sup> (Jewish Hosp. of Cincinnati), many advantages of natural childbirth can be obtained during the first stage of labor by use of alphaprodine hydrochloride (nisentil®) with or without scopolamine, but without barbiturates. He reports observations on 402 term labors with divided doses of 120-360 mg. Mothers experienced euphoria rather than narcosis and were conscious and co-operative throughout labor. The only change in maternal respiratory rates, recorded in about 200 patients, was slowing to normal in those who had been apprehensive. One extremely anxious woman had a convulsion lasting three minutes immediately after a dose of 60 mg. After 3 hours she was given another 30 mg without any reaction and 2½ hours later was delivered of a healthy infant under gas-oxygen anesthesia.

Of the five perinatal deaths, not one could be attributed to the drug. Apnea occurred in two instances, both infants survived and were perfectly normal seven months and two years later. Only 26 infants offered even slight resistance to immediate crying, the longest period being 2½ minutes, all these infants were delivered under gas-oxygen anesthesia. Resuscitation of the other 369 infants (including two sets of twins) was immediate, i.e., within 30 seconds, since low spinal anesthesia has been used, all infants have responded within that time.

If divided doses of 0.5-0.75 mg scopolamine were used as a supplement (almost every patient received at least 0.25 mg), considerable amnesia occurred besides euphoria. No barbiturate was used, and most patients were fully conscious within 10 minutes after anesthesia was stopped. Most satisfactory dosage was initial subcutaneous injection of 30 or 60 mg, depending on weight of the mother, degree

(4) Am. J. Obst. & Gynec. 71:1001-1006, May, 1956.

of apprehension, character and intensity of contractions and estimate of length of further labor. Then 30 mg was given every one to three hours depending on response. In only 18 patients (4.5%) was the drug totally inadequate and possibly these women should have received larger doses.

Principal shortcoming of misentil® was its relative ineffectiveness toward the end of the first stage of labor. This period varied from not at all in over half to about 90 minutes in others. In about 20% of the patients, trichlorethylene inhalations were used to supplement the alphaprodine and in about a third of these intermittent gas oxygen was given with each contraction until dilatation was accomplished and the head was low enough for complete anesthesia and for ceps delivery. Recently low spinal anesthesia has been used in such instances a little earlier than it would ordinarily have been administered.

► [In the absence of control observations one is unable to determine whether or not the results reported are due to the properties of the drug or to its application. The acceptable results may well have been obtained with equally careful administration of such drugs as morphine or meperidine. It is pointed out that the respiratory rate is a poor measure of impaired ventilation—rather pronounced hypoventilation can exist in the presence of a normal respiratory rate.—Ed.]

**Anticholinergic Drugs in Preanesthetic Medication.** After preliminary study of effect of anticholinergic drugs on salivation and heart rate in dogs and comparison of atropine, scopolamine, banthine® and antrenyl® in humans by a blind study,<sup>5</sup> C. R. Stephen, M. A. Bowers, W. K. Nowill and R. C. Martin (Duke Univ.) administered antrenyl® (oxyphenonium bromide) as preoperative medication to about 6,000 patients. The drug was given intravenously, subcutaneously or intramuscularly 5-30 minutes before induction of anesthesia. Parenteral injection was effective in 10-15 minutes. Solutions containing 1 mg/cc proved nonirritating and stable at room temperatures. Dosage range of 0.1-1.5 mg through experience was narrowed to 0.5-0.75 mg as the usual dosage for adults.

Antrenyl® seems to meet adequately the requirements of preanesthetic anticholinergic medication. Troublesome salivary secretions were uncommon even with inexperienced open drop ether administrations. Laryngospasm and bronchospasm were rare though not eradicated. Parasympathetic reflexes involving the cardiovascular system during opera-

tion were infrequent, and incidence was reduced with antrenyl® as compared with atropine. Vagal reflexes when present were abolished rapidly and with some permanence by small doses.

As used in premedication, the drug produced no cerebral sedation. In certain patients a moderately rapid tachycardia followed injection. Of 4,400 anesthetic records, 2.3% showed average increase in pulse rate of 30/minute, 2% showed increase of 40/minute and 1.2% of 50/minute. In most patients with definite tachycardia, the effect persisted three to four hours, clearly demonstrating the length of action of antrenyl®. Pulse rate then returned toward normal gradually.

Since heart rate is controlled primarily by variations in vagal tone, it is reasonable to believe that with an anticholinergic drug, the rate will increase conspicuously in patients with minimal vagal tone and, conversely, may vary little in patients with marked vagal tone. Under these circumstances, an anticholinergic drug that consistently produces some increase in heart rate is serving its function well. A drug that increases heart rate markedly in most patients may be hazardous. In older patients, particularly those with advancing cardiovascular disease and coronary sclerosis, pronounced tachycardia may result in myocardial damage. Considering these factors, the authors believe that antrenyl® is relatively safe in providing optimal anticholinergic effect in human beings for several hours.

**Mechanism of Increased Intracranial Pressure Induced by Morphine.** Morphine causes a rise in cerebrospinal fluid pressure that is particularly dangerous in patients with pre-existing intracranial hypertension. Availability of nalorphine, an effective morphine antagonist, has allowed a new approach to the problem of the way this increased pressure occurs. Arthur S. Keats and John C. Mithoefer<sup>6</sup> (Cooperstown, N. Y.) report effects of morphine and nalorphine on 19 unselected patients without neurologic disease, who were to receive spinal anesthetics through intrathecal catheters for a variety of operations. Mean cerebrospinal fluid pressure in 17 subjects before the experiment was  $237 \pm 11$  mm water, which is higher than the usually accepted normal value and attributable partly to the fact that subjects were supine. Morphine produced the expected rise in pressure.



Nalorphine had similar effect when given initially without prior morphine medication. When morphine was given after nalorphine, a partial blocking effect and smaller rise were observed. Nalorphine given after morphine caused a marked fall in cerebrospinal fluid pressure.

Since ventilatory depression and resultant carbon dioxide accumulation increase intracranial pressure, simultaneous measurements of cerebrospinal fluid pressure, alveolar ventilation and alveolar gas composition were made on two

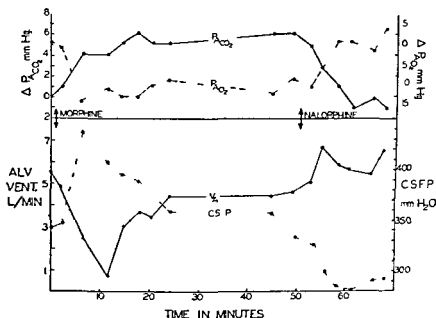


Fig 144—Simultaneous measurements of effect of morphine and nalorphine on cerebrospinal fluid pressure (CSFP), alveolar gas composition ( $P_{ACO_2}$  and  $P_{AO_2}$ ) and alveolar ventilation ( $V_A$ ) in one subject (Courtesy of Keats A. S. and Mithoefer J. C. New England J Med 252 1110 1113 June 30 1955)

subjects (Fig 144). Changes in alveolar ventilation, oxygen and carbon dioxide tensions and cerebrospinal fluid pressure after morphine administration are apparent. Increase in cerebrospinal fluid pressure was associated with a fall in alveolar ventilation and by increase in alveolar carbon dioxide and a fall in alveolar oxygen composition. These changes were reversed by nalorphine.

To test the hypothesis that rise in cerebrospinal fluid pressure is due to respiratory depression, effects of hyperventilation on changes observed after morphine and nalorphine were studied in three subjects. Initial fall in pressure that followed hyperventilation before any drug was administered was interpreted as resulting from decreased cerebral

blood flow secondary to lowered carbon dioxide tension. Simultaneous hyperventilation and intravenous injection of morphine did not increase pressure as long as hyperventilation was continued. When it was stopped, pressure rose. Repeating hyperventilation again caused a fall in pressure, which increased again when hyperventilation was stopped. Administration of nalorphine after morphine lowered cerebrospinal fluid pressure to approximately the level before administration of morphine. Hyperventilation then caused insignificant changes and previously administered nalorphine successfully blocked effects of subsequent administration of morphine.

The efficacy of nalorphine in lowering cerebrospinal fluid pressure after its elevation by morphine suggests its trial under clinical circumstances as an antagonist to this sometimes dangerous morphine effect.

**Further Cerebrospinal Fluid Pressure Studies** Recently Swerdlow and associates reported that levallorphan given before, with or after nisentil® significantly prevented or reversed rise in cerebrospinal fluid pressure which followed administration of the analgesic alone. Mark Swerdlow<sup>7</sup> (Manchester, England) now reports studies on 72 patients (55 men) of antidotal effects of levallorphan and N allylnormorphine on pethidine induced rise in cerebrospinal fluid pressure. Age range was 21-74, average 48.3, average weight was 67 kg, with a range of 45-90.

Patients were premedicated with 5-10 mg morphine and 0.6 mg atropine given subcutaneously one hour before the test. Standard dose of pethidine was 1 mg/kg, dosage of levallorphan was 0.01 mg/kg and of N allylnormorphine, 0.05 mg/kg. Test period was 12 minutes. In 12 patients, the standard dose of pethidine was given, 12 had a mixture of pethidine and N allylnormorphine (20:1) and 12 a mixture of pethidine and levallorphan (100:1). In all these patients, cerebrospinal fluid readings were taken at 1 minute intervals for 12 minutes. In 12 six one minute readings were taken after pethidine and then six more after N-allylnormorphine was injected, in another 12, the procedure was similar, except that the last six readings followed an injection of levallorphan.

Pethidine caused marked rise in cerebrospinal fluid pres-

(7) *Anaesthesia* 11:149-155 April 1956

Nalorphine had similar effect when given initially without prior morphine medication. When morphine was given after nalorphine, a partial blocking effect and smaller rise were observed. Nalorphine given after morphine caused a marked fall in cerebrospinal fluid pressure.

Since ventilatory depression and resultant carbon dioxide accumulation increase intracranial pressure, simultaneous measurements of cerebrospinal fluid pressure, alveolar ventilation and alveolar gas composition were made on two

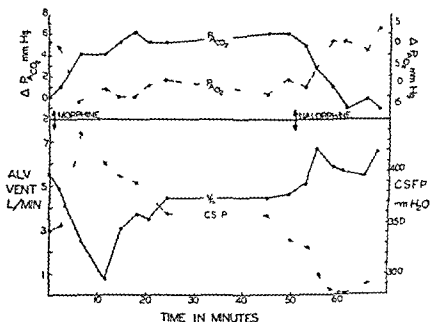


Fig 144—Simultaneous measurements of effect of morphine and nalorphine on cerebrospinal fluid pressure (CSFP), alveolar gas composition ( $P_{ACO_2}$  and  $P_{AO_2}$ ) and alveolar ventilation ( $V_A$ ) in one subject (Courtesy of Keats A S and M thoefler J C New England J Med 252 1110 1113 June 30 1955)

subjects (Fig 144). Changes in alveolar ventilation, oxygen and carbon dioxide tensions and cerebrospinal fluid pressure after morphine administration are apparent. Increase in cerebrospinal fluid pressure was associated with a fall in alveolar ventilation and by increase in alveolar carbon dioxide and a fall in alveolar oxygen composition. These changes were reversed by nalorphine.

To test the hypothesis that rise in cerebrospinal fluid pressure is due to respiratory depression, effects of hyperventilation on changes observed after morphine and nalorphine were studied in three subjects. Initial fall in pressure that followed hyperventilation before any drug was administered was interpreted as resulting from decreased cerebral

blood flow secondary to lowered carbon dioxide tension. Simultaneous hyperventilation and intravenous injection of morphine did not increase pressure as long as hyperventilation was continued. When it was stopped, pressure rose. Repeating hyperventilation again caused a fall in pressure, which increased again when hyperventilation was stopped. Administration of nalorphine after morphine lowered cerebrospinal fluid pressure to approximately the level before administration of morphine. Hyperventilation then caused insignificant changes and previously administered nalorphine successfully blocked effects of subsequent administration of morphine.

The efficacy of nalorphine in lowering cerebrospinal fluid pressure after its elevation by morphine suggests its trial under clinical circumstances as an antagonist to this sometimes dangerous morphine effect.

**Further Cerebrospinal Fluid Pressure Studies** Recently Swerdlow and associates reported that levallorphan given before, with or after nisentil® significantly prevented or reversed rise in cerebrospinal fluid pressure which followed administration of the analgesic alone. Mark Swerdlow<sup>7</sup> (Manchester, England) now reports studies on 72 patients (55 men) of antidotal effects of levallorphan and N-allylnormorphine on pethidine-induced rise in cerebrospinal fluid pressure. Age range was 21-74, average 48.3, average weight was 67 kg, with a range of 45-90.

Patients were premedicated with 5-10 mg morphine and 0.6 mg atropine given subcutaneously one hour before the test. Standard dose of pethidine was 1 mg/kg, dosage of levallorphan was 0.01 mg/kg and of N-allylnormorphine, 0.05 mg/kg. Test period was 12 minutes. In 12 patients, the standard dose of pethidine was given, 12 had a mixture of pethidine and N-allylnormorphine (20:1) and 12 a mixture of pethidine and levallorphan (100:1). In all these patients, cerebrospinal fluid readings were taken at 1 minute intervals for 12 minutes. In 12, six one minute readings were taken after pethidine and then six more after N-allylnormorphine was injected, in another 12, the procedure was similar, except that the last six readings followed an injection of levallorphan.

Pethidine caused marked rise in cerebrospinal fluid pres-

sure for the first seven minutes and a continuing but less steep rise thereafter to the end of the test. N-allylnormorphine, in ratio of 1:20, given with or after pethidine materially prevented or reversed the raised cerebrospinal fluid pressure. Levallorphan, in ratio of 1:100 or 1:50, had little effect whether given with or after the analgesic.

The possibility cannot be excluded that the relative ineffectiveness of levallorphan was due to the fact that molar concentration of pethidine was three times that of nisentil<sup>3</sup> (against which levallorphan was effective in preventing or reversing rise in cerebrospinal fluid pressure). Since in all probability, the effect of the antagonist can be explained by competition of similar substrates for a common receptor, the ratio of molar concentrations of the narcotic and the antagonist is important.

Swerdlow suggests that it would be logical and useful to administer N-allylnormorphine with pethidine when the latter is used during neurosurgical operations. This should minimize the rise in intracranial tension while sparing much of the analgesic action of pethidine.

► [The preceding abstracts corroborate other observations in that the restoration of adequate ventilation with its associated elimination of carbon dioxide retention reduces the increase in intracranial pressure associated with the use of narcotic drugs. However it seems that prevention of hypoventilation by limited use of narcotics in circumstances in which increased spinal fluid pressure is detrimental or treatment of hypoventilation by assisted or controlled artificial ventilation would be more appropriate than an attempt to balance narcotic and antagonist. In the light of evidence now available that the antagonists are capable of producing significant depression of ventilation precise adjustment of a mixture of narcotic and antagonist is mandatory but difficult to achieve.—Ed.]

**Effect of Preanesthetic Medications on Blood Level of 17-Hydroxycorticosteroids** was investigated in 65 patients (35 females) aged 20-45, by Ephraim S. Siker, Elia Lipschitz and Robert Klein<sup>8</sup> (Univ. of Pittsburgh). Saline, atropine and scopolamine produced no change in blood levels of free corticoids. Though mean value in the morphine group dropped from 12 to 8  $\mu\text{g}/100\text{ ml}$ , the change was not statistically significant. The only significant change ( $P < 0.02$ ) occurred in patients who received pentobarbital. Neither morphine, atropine nor pentobarbital inhibited rise in serum levels of free corticoids following administration of ACTH.

The findings suggest that pentobarbital probably inter-

feres with release or formation of ACTH, and morphine probably has a similar effect. The consistent pentobarbital values may reflect the more uniformly sedative effect of this agent as compared with that of morphine.

Fall in serum levels of free corticoids that follow the usual combination and dosage of premedicating agents may be due to an altered hypothalamic threshold. This was substantiated in a preliminary investigation in which premedicating agents did not inhibit the adrenocortical response to anesthesia.

Anxiety, apprehension and concern may be marked in patients about to have surgery. In one reported study, urinary 17-hydroxycorticosteroids in 10 healthy subjects rose from values of 1.47  $\mu\text{g}/\text{minute}$  while tranquil to values of 5.6-8.3  $\mu\text{g}/\text{minute}$  when apprehension, anger or excitement were provoked. If a relation exists between titer of serum levels of free corticoids and these subjective emotions, elevation of the former would be expected to follow emotional stimulation, and adequate sedation should produce a fall.

**Effect of Nisentil® Hydrochloride and Lorfan Tartrate on Respiration during Nitrous Oxide-Oxygen Anesthesia** was studied in 280 surgical cases by Edith R. Kepes and Bernard R. Margolius<sup>9</sup> (Montefiore Hosp., New York). In the first part of the investigation, respiratory rate, minute volume and tidal volume were recorded, and alveolar ventilation was calculated preoperatively, at the end of surgery and one hour after termination of anesthesia for 80 anesthetized patients who required minimal relaxation and who received premedication with only atropine or scopolamine. Thiopental (pentothal®) sodium or a premixed solution of the analgesic, alphaprodine (nisentil®) hydrochloride and the narcotic antagonist levallorphan (lorfan) tartrate, was used for induction. Anesthesia was maintained with N<sub>2</sub>O-O<sub>2</sub> supplemented with alphaprodine hydrochloride and levallorphan tartrate or with thiopental sodium by various techniques.

In almost every instance the initial dose of alphaprodine hydrochloride produced severe respiratory depression, which was easily controlled by levallorphan tartrate. In patients who received the analgesic with the antagonist, severe depression was prevented though moderate depression, which lasted two to five minutes, occurred after the first

(9) Am J Surg 91:761-769 May 1956

injection and after institution of continuous drip of the premixed combination of alphaprodine hydrochloride and levallorphan tartrate. Subsequently, respiratory function was adequate. Thiopental sodium alone without analgesic or antagonist caused shallow respirations.

Continuous drip of premixed alphaprodine hydrochloride and levallorphan tartrate caused no depression of alveolar ventilation. In contrast, this ventilatory measurement was significantly decreased one hour postoperatively when sodium pentothal was used for induction, followed by intermittent injections of alphaprodine-levallorphan mixture, and when thiopental was used alone. The reductions were significant statistically but not clinically.

In the second part of the study, respiratory rates were determined initially, at frequent intervals and terminally in 200 unselected surgical patients who received premedication with meperidine (demerol®) hydrochloride, atropine or scopolamine, and, in 142 instances, also with secobarbital® (seconal®) sodium. Thiopental sodium was used in all patients for induction and a continuous drip of an alphaprodine hydrochloride-levallorphan tartrate mixture (50:1) for supplementation. Additional doses of thiopental sodium were given as needed. Succinylcholine (anectine®) hydrochloride was used for intubation and relaxation. These patients tolerated appreciably larger doses of alphaprodine hydrochloride than can be given with impunity to patients who do not receive levallorphan tartrate conjointly. Reactivity of all 200 patients on completion of surgery was excellent.

No major complications were noted in any patient. Supplementation of N<sub>2</sub>O-O<sub>2</sub> anesthesia with a continuous drip of a premixed solution of alphaprodine hydrochloride and levallorphan tartrate in a 50:1 ratio provided satisfactory analgesia, with only transient respiratory depression and prompt postoperative recovery.

► [Calculation of alveolar ventilation, as applied in this report, assumes that dead space does not change. Since it is possible that the dead space did change with a change in respiratory rate, the observations may be in error.—Ed.]

**Comparative Effects of New Narcotic Antagonist (Levallorphan Tartrate) on Respiratory Responses to Carbon Dioxide during Narcotic and Barbiturate Depression in Anesthetized Man.** There is now ample evidence that in man N-allylnormorphine effectively antagonizes the respiratory

depressant effects of morphine and other narcotics, though itself a respiratory depressant

Charles M Landmesser, Paul F Formel and J Gerard Converse<sup>1</sup> (Albany, N Y) studied 15 thyroidectomy patients, 5 receiving l-dromoran, 5, morphine, and 5 nembutal,\* besides atropine or scopolamine as premedication and the same drug again intravenously just before or during surgery or at both times N.O.O. endotracheal anesthesia was given Respirations were measured at end of surgery on the circle system with 100% oxygen Tracings were obtained with and without CO<sub>2</sub> rebreathing, before and after intravenous injection of levallorphan tartrate Data from the last minute of each test period were used, and arterial blood samples were collected simultaneously

Plotting average group values for respiratory rate, tidal and minute volume and alveolar ventilation ratio against corresponding values for arterial CO<sub>2</sub> tension demonstrated that, in the l dromoran and morphine groups, the threshold of respiratory response to CO<sub>2</sub> decreased after levallorphan whereas in the nembutal\* group the threshold increased after levallorphan administration Arterial O<sub>2</sub> saturation was adequate at all times Blood pressure and pulse rate were not affected by levallorphan

The study showed that levallorphan, the allyl derivative of l dromoran antagonizes the respiratory depressant effect of its parent drug and of more distantly related morphine The degree of initial hyperpnea following the narcotic antagonist is more dependent on the amount of CO<sub>2</sub> retained from the narcotic depression than on the degree of structural similarity between antagonist and depressant The CO<sub>2</sub> tension pH and increased respiratory minute volumes in the nembutal\* group indicated that neither the same kind nor degree of respiratory depression existed Levallorphan, as naline,\* acts by competing for the effector cells of its related narcotics, probably in the respiratory center, which then again becomes more sensitive to CO<sub>2</sub> In barbiturate depression narcotic antagonists increase the degree of depression by virtue of their own depressant effect

► [It is interesting that the authors state that the antagonist failed to antagonize respiratory depression induced by nembutal\* in view of the fact that their data indicate that no respiratory depression existed in the patients receiving nembutal\*—Ed]



**Effect of Nisentil,\* Meperidine and Morphine on Respiration in Man** Louis R Orkin, Robert K Egge and E A Rovenstine<sup>2</sup> (New York Univ) investigated ventilation and oxygen uptake in 30 patients, 10 of whom were given 10 mg morphine, intravenously (2.5 mg/cc/minute), 10, 100 mg meperidine intravenously (25 mg/cc/minute) and 10, 60 mg nisentil<sup>®</sup> subcutaneously in a single injection. Respirations were recorded on a Benedict-Roth spirometer, employing oxygen and carbon dioxide absorption. Effective tidal volumes were assumed to be 150 cc less in males and 100 cc less in females than those measured. The same correction factor was applied to effective minute volume. Recordings were followed for an hour.

After morphine or meperidine respiratory tidal volume and rate immediately fell markedly. Tidal volume then returned to above normal with morphine, whereas the rate remained slow. After meperidine, the rate returned to above normal values and the tidal volume remained reduced. Minute volume was more depressed by meperidine than by morphine in the doses used. Nisentil<sup>®</sup> reduced tidal volume and rates in 10-15 minutes. Depression of minute volume was about the same as under meperidine. Oxygen uptake was not significantly altered by these analgesic agents. Ventilation data were not significantly affected by age or sex. The best sign of depressed respiration was waxing and waning of the depth and a similar variation in rhythm, of respiration. The study emphasizes the respiratory depressant effect of meperidine and redemonstrates the difficulty of producing hypoxia by hypoventilation produced by narcotics.

**Respiratory Hazards of Opiates and Other Narcotic Analgesics** were analyzed by James E Eckenhoff, Martin Helrich, Muriel J D Hege and Richard E Jones<sup>3</sup> (Univ of Pennsylvania) from data accumulated during a study of the effect of anesthetic agents on development of respiratory acidosis. They tested response of the respiratory center to endogenously accumulated CO<sub>2</sub> before and at intervals after administration of various drugs.

In all 21 subjects to whom opiates or opiate like drugs

(2) Anesthesiology 16:699-707, September 1955

(3) Surg. Gynec. & Obst. 101:701-708, December 1955

were given, a rise in alveolar  $\text{Pco}_2$ , with a range of 2-13 mm. (average, 5.7 mm.), was demonstrated. Decrease of respiratory minute volume was observed in 19 subjects. Respiratory tidal volume was definitely diminished in 15 of 22, with an equivocal change in 5 others.

Respiratory rate was notably deficient as a guide to respiratory depression from opiates; this was present in only 6 of 21 subjects. Eleven had no change or an equivocal one, and four developed a more rapid rate of respiration. One had a reduction of 28% in minute volume and of 31% in tidal volume, despite slight elevation in respiratory rate. Respiratory response to endogenously accumulated  $\text{CO}_2$  was depressed after opiates in all but one patient (studied for only one hour after morphine was given). Usually this response continued to be diminished after other respiratory measurements returned to normal.

Respiratory response of three subjects who received barbiturates contrasted sharply with that noted after opiates. None showed significant alteration in  $\text{Pco}_2$ , there was no definite pattern of respiratory depression evidenced by respiratory rate, tidal or minute volume, nor was response to  $\text{CO}_2$  reduced after the barbiturate. Sedative effect was unquestionable, since sleep was produced in all three.

Sensitivity of the respiratory center to  $\text{CO}_2$  is a protective mechanism, and man has sufficient reserve to withstand considerable depression without harm. However, if opiates are given to patients with diminished reserve (e.g., patients with pulmonary emphysema),  $\text{Pco}_2$  is further increased, respiratory response to  $\text{CO}_2$  further diminished, respiratory acidosis enhanced and a potentially hazardous situation precipitated. Any patient in whom blood supply or function of the respiratory center is impaired is a potential candidate for the same hazard. Depression of response of respiration to  $\text{CO}_2$  is prolonged after opiates, often persisting after respiration seems to have returned to normal.

After use of opiates, man can withstand other depressants less well. Patients to whom opiates are given preanesthetically often have apnea after induction of cyclopropane anesthesia. If a patient is under the influence of a depressant such as a general anesthetic, an opiate may lead to unexpectedly acute respiratory depression.

The important action of opiates is analgesic. Barbiturates seem less hazardous and equally effective in producing sleep and relieving emotional stress. Routine use of opiates as preanesthetic medication is a questionable practice, but other difficulties may arise because of their omission, these observations require further assessment. Opiate administration requires individualization, with full cognizance of what the chosen narcotic may do to the particular patient, and reasonably constant surveillance.

► [One should be careful to heed the remarks of the authors regarding the value of opiates in premedication. Although the evidence is convincing that opiates contribute to depression of ventilation, one may easily compensate for hypoventilation and the patient still benefit from the use of opiates as a part of premedication.—Ed.]

**Nonbarbiturate Sedatives** Although barbiturates with short, medium and long-acting properties are available and can be given orally, intramuscularly and intravenously, in certain circumstances, such as idiosyncrasy, toxic rashes and addiction, their use is undesirable. Long continued consumption of barbiturates may induce insomnia, depression and anxiety, and serious withdrawal symptoms may occur if they are discontinued abruptly. According to W. Gordon Sears,<sup>4</sup> alternative drugs may be of equal or superior value, if carefully selected.

The most important of the older sedatives, excluding opium and its derivatives, are hyoscine hydrobromide, paraldehyde, chloral hydrate and bromides. Hyoscine (scopolamine) hydrobromide is particularly useful in conditions with motor agitation, i.e., acute mania, delirium and delirium tremens. It may be combined with morphine or alternated with other drugs. The maximal dose of 1/30 gr (2 mg) should not be exceeded. Hyoscine orally may be effective in prevention and treatment of travel sickness. Paraldehyde is rapid and safe and one of the most useful sedatives for restless, noisy or delirious patients. It is given intramuscularly, 5-10 ml, in delirium tremens 15-20 ml may be required. Chloral hydrate, the first synthetic hypnotic, has properties similar to those of barbiturates. It is safe when given well diluted to avoid irritation of the digestive tract. Chloral is useful in anxiety states with marked emotional agitation, also in insomnia associated with acute painless conditions. The usual maximal adult dose is 30 gr (2

Gm) Infants and children tolerate it well, 1 gr (60 mg) may be given every four to six hours to very young infants. Bromides and sulfonamides\* have many disadvantages and are now rarely used.

The action of monoureides (barbiturates are diureides) is comparable to that of chloral hydrate. One of these, sedormid,\* is not recommended because prolonged administration may cause thrombocytopenia. Bromaletone and carbromal may be prescribed separately but are combined in various proprietary preparations, sometimes with other therapeutic substances, e.g., persomnia, sedaltine and noctynol. The latter two may be given to children in suitable amounts.

Several new nonbarbiturate drugs have been recommended as sedatives and hypnotics, although clinical experience with them is insufficient for final evaluation. Glutethimide (doriden\*) is a rapid-acting hypnotic inducing sleep in 20-30 minutes, with medium duration averaging 6 hours. Initial dose of two tablets, each 0.25 Gm, may later be reduced to one tablet. Other drugs in this group are noludar\* valmid, dipipanone and methylpentynol.

Some drugs used for other purposes also have valuable sedative properties. e.g., antihistamines, chlorpromazine, mephenesin and rauwolfia derivatives. Antihistamines with sedative effects include diphenhydramine, mepyramine maleate, chlorcyclizine and promethazine. Chlorpromazine has a place in treatment of certain psychoneuroses, anxiety states and hysteria. Agitated elderly patients may benefit considerably, though symptoms may be exacerbated during the first few days. Dosage must be individualized beginning with 25 mg three times daily and increasing by 25 mg to a maximum of 200-300 mg/day. Toxic effects of chlorpromazine include jaundice (2%), agranulocytosis (rare) and skin sensitization. Mephenesin is a muscle relaxant that may be combined advantageously with other drugs for relief of tension. Rauwolfia and reserpine are useful not only in mental tension of hypertension but also in other anxiety states. e.g., menopausal conditions, premenstrual tension and hyperthyroidism. In these cases it usually has little effect on normal blood pressure. Dose is adapted to individual requirements at about 0.25 mg four times daily. Benactyzine (suavitil) is a new anticholinergic substance and

The important action of opiates is analgesic. Barbiturates seem less hazardous and equally effective in producing sleep and relieving emotional stress. Routine use of opiates as preanesthetic medication is a questionable practice, but other difficulties may arise because of their omission, these observations require further assessment. Opiate administration requires individualization, with full cognizance of what the chosen narcotic may do to the particular patient, and reasonably constant surveillance.

► [One should be careful to heed the remarks of the authors regarding the value of opiates in premedication. Although the evidence is convincing that opiates contribute to depression of ventilation, one may easily compensate for hypoventilation and the patient still benefit from the use of opiates as a part of premedication.—Ed.]

**Nonbarbiturate Sedatives** Although barbiturates with short, medium and long acting properties are available and can be given orally, intramuscularly and intravenously, in certain circumstances, such as idiosyncrasy, toxic rashes and addiction, their use is undesirable. Long continued consumption of barbiturates may induce insomnia, depression and anxiety, and serious withdrawal symptoms may occur if they are discontinued abruptly. According to W. Gordon Sears,<sup>4</sup> alternative drugs may be of equal or superior value, if carefully selected.

The most important of the older sedatives, excluding opium and its derivatives, are hyoscine hydrobromide, paraldehyde, chloral hydrate and bromides. Hyoscine (scopolamine) hydrobromide is particularly useful in conditions with motor agitation, i.e., acute mania, delirium and delirium tremens. It may be combined with morphine or alternated with other drugs. The maximal dose of 1/30 gr (2 mg) should not be exceeded. Hyoscine orally may be effective in prevention and treatment of travel sickness. Paraldehyde is rapid and safe and one of the most useful sedatives for restless, noisy or delirious patients. It is given intramuscularly, 5-10 ml, in delirium tremens 15-20 ml may be required. Chloral hydrate, the first synthetic hypnotic, has properties similar to those of barbiturates. It is safe when given well diluted to avoid irritation of the digestive tract. Chloral is useful in anxiety states with marked emotional agitation, also in insomnia associated with acute painless conditions. The usual maximal adult dose is 30 gr (2

Gm) Infants and children tolerate it well, 1 gr (60 mg) may be given every four to six hours to very young infants. Bromides and sulfonal<sup>8</sup> have many disadvantages and are now rarely used.

The action of monoureides (barbiturates are diureides) is comparable to that of chloral hydrate. One of these, sedormid,<sup>9</sup> is not recommended because prolonged administration may cause thrombocytopenia. Bromvaletone and carbromal may be prescribed separately but are combined in various proprietary preparations, sometimes with other therapeutic substances, e.g., persomnia, sedaltine and noctynol. The latter two may be given to children in suitable amounts.

Several new nonbarbiturate drugs have been recommended as sedatives and hypnotics, although clinical experience with them is insufficient for final evaluation. Glutethimide (doriden<sup>®</sup>) is a rapid-acting hypnotic inducing sleep in 20-30 minutes, with medium duration averaging 6 hours. Initial dose of two tablets, each 0.25 Gm, may later be reduced to one tablet. Other drugs in this group are noludar,<sup>®</sup> valmid, dipipanone and methylopentynol.

Some drugs used for other purposes also have valuable sedative properties, e.g., antihistamines, chlorpromazine, mephenesin and rauwolfia derivatives. Antihistamines with sedative effects include diphenhydramine, mepyramine maleate, chlorcyclizine and promethazine. Chlorpromazine has a place in treatment of certain psychoneuroses, anxiety states and hysteria. Agitated elderly patients may benefit considerably, though symptoms may be exacerbated during the first few days. Dosage must be individualized, beginning with 25 mg three times daily and increasing by 25 mg to a maximum of 200-300 mg/day. Toxic effects of chlorpromazine include jaundice (2%), agranulocytosis (rare) and skin sensitization. Mephenesin is a muscle relaxant that may be combined advantageously with other drugs for relief of tension. Rauwolfia and reserpine are useful not only in mental tension of hypertension but also in other anxiety states, e.g., menopausal conditions, premenstrual tension and hyperthyroidism. In these cases it usually has little effect on normal blood pressure. Dose is adapted to individual requirements at about 0.25 mg four times daily. Benactyzine (suavitil) is a new anticholinergic substance said

to raise the threshold for irritant stimuli. Dose is 1-3 mg. three or four times daily.

The younger generation of physicians might be reminded that the best nightcaps are "milk for the young, alcohol for the elderly."

---

## VENTILATION

**Etiologic Factors Affecting Pulmonary Artery Flow with Controlled Respiration.** Effect of positive pressure lung inflation on pulmonary blood flow was studied by Charles A. Hubay, Gerhard A. Brecher and Frederick L. Clement<sup>5</sup> (Western Reserve Univ.) in acute open-chest animal experiments, in which flow and pressure changes were correlated. The purpose was to determine if pulmonary blood flow is reduced by increase in pulmonary bed resistance or by impairment of venous return when lungs are inflated by positive pressure. Pulmonary artery blood flow was directly measured when blood flowed either through the lungs or bypassed the lungs through tubing of constant resistance.

Figure 145 shows two segments of an original record illustrating effect of positive pressure lung inflation on phasic blood flow in right and left pulmonary arteries. Segment A is a control record taken with atmospheric pressure in the airway. Calculated mean flow through the left pulmonary artery was 525 cc./minute; through the right pulmonary artery, 638 cc./minute. Total right heart output was 1,163 cc./minute. Segment B was taken at the end of positive pressure lung inflation which lasted 3 seconds, during which airway pressure rose to 210 mm. water. During lung inflation, the following changes were observed. (1) Mean left pulmonary artery flow decreased to 437 cc./minute, or 16.7%. (2) Mean right artery flow decreased to 444 cc./minute, or 30.3%. (3) Total right heart output was reduced by 24.2%. (4) Aortic pressure rose from 144/123 mm. Hg to 150/125 mm. (5) Right intraventricular pressure increased from 415/35 mm. water to 425/75 mm. (6) Left atrial pressure rose from 51 mm. water to 77 mm. (7) Right atrial pressure increased from 38 mm. water to 73 mm. during lung inflation.

---

(5) Surgery 38 215-227, July, 1955

Comparison of blood flows when blood was shunted or not shunted showed that the major portion of flow reduction during mild positive pressure lung inflation was caused by increased resistance in the pulmonary beds. A minor part of flow reduction could be attributed to mechanical factors outside the pulmonary circulation. Evidence for existence of these mechanical factors was obtained by correlating

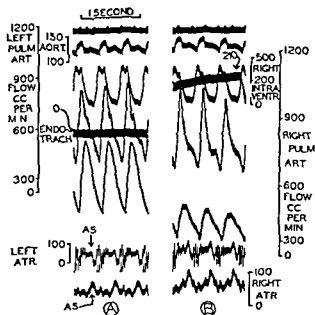


Fig 145—Effect of positive pressure lung inflation on right and left pulmonary artery flow in open chest. Segment A flow and pressure tracings during atmospheric airway pressure marked as endotracheal O. Segment B same tracings during lung inflation with endotracheal pressure of 210 mm water. Sequence of tracing is from top to bottom: time, aortic pressure in mm Hg, right intraventricular pressure in mm water, left pulmonary artery flow in cc/minute, endotracheal pressure in mm water (thick horizontal line), right pulmonary artery flow in cc/minute, left and right atrial pressures in mm water. AS is atrial systole. Time between end of segment A and beginning of segment B is 2.3 seconds. (Courtesy of Hubay C. A. et al. *Surgery* 38:215-227, July, 1955.)

pulmonary blood flow with pressures in both atria, the right ventricle, pulmonary artery and aorta.

This study demonstrated that mild positive pressure lung inflation with dogs in a supine position and after bilateral thoracotomy, results in decreased blood flow, due to compression and distortion of the heart and great vessels. In clinical practice, the commonly used lateral decubitus position may accentuate compression and distortion effects of lung inflation and interfere with circulation. Admittedly, in patients with adequate circulatory reserve, compensation for such derangements is commonly observed, but in patients who have had considerable blood loss or who are



otherwise in poor circulatory condition, the effect may be so detrimental as to threaten life.

**Carbon Dioxide Homeostasis during Anesthesia.—III. Ventilation and carbon dioxide elimination.**—By application of the infra-red carbon dioxide analyzer and the pneumotachograph, James O. Elam and Elwyn S. Brown<sup>6</sup> (Buffalo, N. Y.) demonstrated inter-related mechanisms governing transfer of carbon dioxide from tissues of anesthetized patients (Fig. 146). Maintenance of normal  $\text{CO}_2$  tension depends on a balance between its production and elimination.

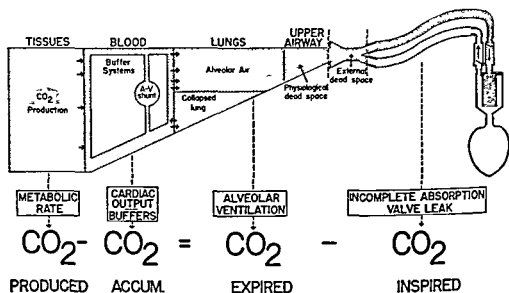


Fig 146.—Factors effecting carbon dioxide elimination during closed system anesthesia (Courtesy of Elam, J. O., and Brown, E. S.: *Anesthesiology* 17:116-127, January, 1956.)

In absence of  $\text{CO}_2$  rebreathing, the patient's production of  $\text{CO}_2$  determines the requirement for alveolar ventilation.  $\text{CO}_2$  production of anesthetized adults varies between 60 and 500 cc./minute, depending primarily on the anesthetic agent. Alveolar ventilation required to maintain  $\text{CO}_2$  homeostasis may therefore vary between 1 and 8.6 L./minute. During demerol®-scopolamine anesthesia, normal alveolar  $\text{CO}_2$  tension may be maintained with alveolar ventilation as low as 1 L./minute and a respiratory rate of 3.3/minute. With plane 3 ether anesthesia, normal alveolar  $\text{CO}_2$  tension was not maintained with alveolar ventilation of 4.9 L./minute and a respiratory rate of 34/minute. Carbon dioxide ac-

(6) *Anesthesiology* 17 116-127, January, 1956.

accumulation was consistently found during ether anesthesia at surgical planes

In the presence of CO<sub>2</sub> rebreathing, requirement for alveolar ventilation is determined not only by the patient's production of CO<sub>2</sub> but also by concentration of inspired CO<sub>2</sub>. With increased rate of production during ether anesthesia, increase in inspired CO<sub>2</sub> concentration imposes an additional burden on ventilation. Tachypneic breathing during ether anesthesia is not suited to an efficient response to inspired CO<sub>2</sub>. Approximately 1 L of dead space ventilation is wasted for each liter of alveolar ventilation. With sodium pentothal,\* this inefficiency may be doubled. By contrast, slow deep breathing during demerol\*—scopolamine anesthesia affords an economical response to inspired CO<sub>2</sub>, with about 0.5 L of dead space expended per liter of alveolar ventilation.

An adequate ventilatory response to inspired CO<sub>2</sub> concentrations below 4.2% was intact in planes 1 and 2 ether anesthesia, in demerol\*—scopolamine nitrous oxide anesthesia, and in pentothal\*—nitrous oxide anesthesia of moderate depth. Ventilatory response to CO<sub>2</sub> in plane 3 ether anesthesia was not sufficient to prevent accumulation of carbon dioxide. The patient's alveolar carbon dioxide tension may be maintained at normal value provided rebreathing of CO<sub>2</sub> is eliminated and ventilation is assisted when agents are used that produce weakness or paralysis of respiratory muscles.

*IV Evaluation of partial rebreathing system*—Elam and Brown<sup>7</sup> made the evaluation from the standpoint of inspiratory CO<sub>2</sub> concentrations provided by inflow rates comparable to minute ventilation of patients anesthetized with ether or demerol\*—scopolamine. Complete removal of CO<sub>2</sub> from the bag in the partial rebreathing system is not obtained by these inflow rates. Inflow rates comparable to minute ventilation as measured before rebreathing resulted in inspired concentrations of 1.2–4.2%, averaging 2%. Degree of CO<sub>2</sub> rebreathing produced by this system was greater with ether anesthesia than with opiate depression. In all patients, use of the method evoked increase in ventilation. Inflow rates of 15 L/minute are not sufficient to prevent accumulation of CO<sub>2</sub> in all patients, and the commonly used

(7) *Anesthesiology* 17:128–134, January 1956.

inflow rate of 10 L/minute may result in concentrations above 4% of inspired  $\text{CO}_2$  despite excessive hyperventilation

Use of inflow rates sufficiently high to eliminate expired  $\text{CO}_2$  from air inspired is impractical and inefficient. A more feasible means of eliminating rebreathing of  $\text{CO}_2$  is use of valves that convert existing rebreathing assemblies to non-rebreathing units. Inflow rates no greater than the patient's minute ventilation are then sufficient, and inspired  $\text{CO}_2$  concentration is reduced to zero.

► [The assumption that the changes observed were a function of production of carbon dioxide is open to question. Observations of others made on patients in similar circumstances do not substantiate the findings reported.—Ed.]

**Use of Exsufflation with Negative Pressure in Postoperative Patients** Edward K. Williams and Duncan A. Holaday<sup>8</sup> (New York) obtained arterial blood  $\text{CO}_2$  and  $\text{O}_2$  contents and plasma pH in 10 patients, before, during and after exsufflation with negative pressure (EWNP). Seven patients had had abdominal operations and were studied as soon as possible after termination of anesthesia, during the period when mixed respiratory and metabolic acidosis may exist. Three nonsurgical patients with acidosis were studied, two had advanced pulmonary emphysema and one had mild uncompensated metabolic acidosis of undetermined origin. Observations were also made on effects of EWNP on 15 surgical patients who required treatment for retained bronchial secretions one or more days after operation.

The effectiveness of EWNP in removing retained bronchial secretions from patients with fresh operative wounds was clearly demonstrated. The exsufflator contains a valve which instantaneously reverses flow of air between the apparatus and the lungs, resulting in abrupt expulsion of air and retained secretions. Imposition of any obstruction, such as a partially closed glottis, retracted tongue or closed lips, impairs efficiency of EWNP. Most conscious patients were able to carry out the procedure by themselves when the apparatus was left at the bedside. Abdominal or chest wound pain was less during EWNP than during spontaneous coughing. No complication attributable to EWNP occurred.

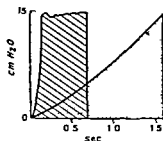
Despite large tidal volumes obtained during EWNP,

pCO<sub>2</sub> did not fall below 30 mm Hg and arterial oxygen saturation rose above 90% in only 3 of 10 patients. Arterial blood gas values reverted toward pretreatment levels promptly.

It seems likely that rapid flow rates developed during EWNP would favor early expansion of portions of the lung with lowest resistance to flow. Overdistention of such areas through distortion of adjacent areas would increase tendency to uneven ventilation. Assuming mixed venous blood to be 70% saturated and blood returning from ventilated alveoli to be 100% saturated, failure to ventilate 25% of the perfused alveoli would result in a mean arterial saturation of 80%, which was the average saturation obtained.

**Testing Apparatus for Intermittent Positive Pressure Respiration.** Influence of Inspiratory Pressure Wave Form. J M K Spalding and S A Young<sup>9</sup> (Oxford Univ.) emphasize that apparatus for providing artificial respiration by intermittent positive pressure

Fig 147—Inspiratory pressure wave forms required to provide tidal volume of 500 ml. Inspirations last less than half as long with the square curve as with wave form IV and mean pressure is lower. (Courtesy of Spalding J M K and Young S A. *Lancet* 2:227-229, July 30, 1955.)



must be thoroughly tested before being approved for clinical use. They cite the fact that at least one apparatus could not provide the minimum ventilation required by some patients, but was widely distributed before this was found out.

A model lung, consisting of a constriction and what is, in effect, a spring-loaded piston, is suitable for laboratory testing such apparatus. Investigations with this device show that a tidal volume of 500 ml can be provided in 0.7 second by the type I pressure wave form (square wave), but that with wave form IV (gradual rise of pressure) 1.6 seconds are required for the same tidal volume. Since inspiration is less than half as long with wave form I, it is preferable from the standpoint of a long period of expiration. Figure 147 shows inspiratory pressure wave forms of types I and IV required to give a tidal volume of 500 ml. Mean pressure with wave form I is 84% of that with wave form IV, there-

(9) *Lancet* 2:227-229, July 30, 1955.

fore wave form J also better fulfills a second requirement for minimizing strain on the circulation, i e, that mean pressure in face mask or tracheal tube must be as small as possible

Apparatus for prolonged artificial respiration by intermittent positive pressure should be designed to give a square wave form This is achieved by rapid onset to the pressure curve, and a gradual rise at the beginning of inspiration should be avoided Testing 10 consecutive paralyzed patients with intermittent positive pressure respiration indicated that a square wave form is clinically satisfactory and comfortable for the patient A pressure wave form of type I from a Radcliffe respiration pump or similar gravity operated pump was used in all cases Except in the first case, duration of inspiration was about 0.85-1.10 seconds at respiratory rates of 13-22/minute Only one patient died while receiving artificial respiration, from intense hemorrhagic consolidation of five sixths of the lungs due to inhalation of vomit before coming under treatment

**Practical Aspects of Carbon Dioxide Absorption** Elwyn S Brown and James O Elam<sup>1</sup> (New York) tested the absorption efficiency of circle absorbers The effective air space of existing circle absorbers is less than a tidal volume of 500 cc because of deficient size or channeling of expired air through preferential paths, as in the Heidbrink 9B and Chicago absorbers Immediate CO<sub>2</sub> accumulation in closed circle systems is prevented by high activity of fresh absorbents

At a tidal volume of 500 cc respiratory rate of 15/minute and CO<sub>2</sub> production rate of 280 cc/minute, an exit CO<sub>2</sub> concentration of 0.5% as end point can be achieved for 4¾ hours in each half of the Heidbrink 9B, 4¼ hours for the Foregger CF no 2 (large), 3¾ hours for the Foregger no 1 and 1½ hours for the Foregger CF no 2 (small) Time efficiencies for each absorber were less when baralyme was used Under the given conditions, one hour of useful life was obtained per 100 Gm soda lime Heidbrink 9B yields less than that because of channeling Increases of tidal volumes and increases in CO<sub>2</sub> production reduced the time efficiencies of absorbers due to overloading If failure of a circle to remove all CO<sub>2</sub> during hyperventilation alone oc-

(1) New York J Med 55 3436-3442 December 1955

curs,  $\text{CO}_2$  accumulation may be postponed, to develop rapidly as terminal exhaustion of the overloaded absorber occurs. Incompetence of breathing valves and insufficient moisture content of soda lime also may be to blame for  $\text{CO}_2$  accumulation. Backflow leaks defeat the potential efficiency of the circle absorber.

Indicators are of no advantage in present systems. Semi-closed systems with a pop-off valve between patient and absorber may increase time efficiency in proportion to the

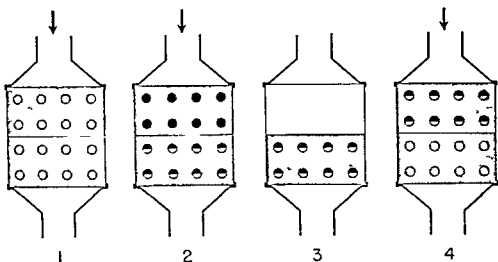


Fig. 148—Depletion and replacement of absorbent in double reversible canister. Absorbent in upper half is exhausted first. When the indicator has changed in this portion, the lower reserve half of absorbent is only partially used. After the upper half is refilled with fresh absorbent, the canister is reversed so the previously partially used absorbent is used to completion. (Courtesy of Brown, E. S., and Elam, J. O. New York J. Med. 55:3436-3442, December, 1955.)

rate of inflow gas, increasing the useful life of the absorber two to three times. If, in this technic, gas escapes after flowing through the absorber, the only advantage of the semi-closed system in  $\text{CO}_2$  removal is in the dilution effect of high inflow rates. Double reversible canisters large enough to accommodate inter- and intragranular air space of two tidal volumes (1,000 cc) are recommended (Fig. 148).

**Diffusion Anoxia.** Bernard Raymond Fink<sup>2</sup> (Columbia Univ.), noting that a discernible degree of cyanosis often develops in patients during recovery from nitrous oxide-oxygen anesthesia, explains the anoxia in terms of the outward diffusion of nitrous oxide from the alveoli, which lowers the alveolar partial pressure of oxygen. At the conclu-

(2) *Anesthesiology* 16:511-519, July, 1955.

sion of anesthesia, the alveolar partial pressure of oxygen and nitrogen is reduced in proportion to the partial pressure of nitrous oxide in the alveoli, which is considerable since nitrous oxide is about 20 times more soluble in blood than oxygen, and at anesthetic levels about 30 ml. is found in 100 ml. blood.

Arterial oxygen saturations, measured in eight patients for 10 minutes during and after nitrous oxide anesthesia

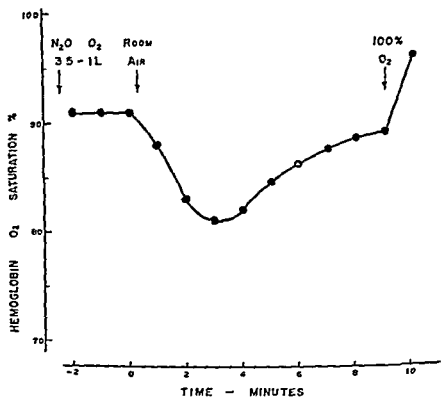


Fig. 149—Arterial oxygen saturation during recovery from nitrous oxide-oxygen anesthesia (Courtesy of Fink B R Anesthesiology 16 511 519, July, 1955)

(75% N<sub>2</sub>O, supplemented before measurements began with thiopental) fell 4.5-10.3% (average 7.9%) (Fig. 149). Spirometric recordings in three patients showed that, during anesthesia, volume of inspiration exceeded that of expiration, suggesting continued absorption of nitrous oxide, whereas during recovery, expiration exceeded inspiration by more than 10% in the first 10 minutes, the excess representing the volume of nitrous oxide eliminated (Fig. 150). Under observed conditions, alveolar oxygen pressure probably fell to 85 mm Hg, representing about 92% saturation of hemoglobin. Blood gas concentration, pulmonary blood flow, ven-

tilation and functional residual air—all affect the partial pressure of gas-oxygen in the lungs

Diffusion anoxia may occur with any anesthetic agent, but will be greater the less soluble the agent in blood and hence the higher the alveolar tension. Effects of two simultaneous anesthetic gases on the  $P_{O_2}$  are additive. Hence diffusion anoxia is especially marked in patients anesthetized with cyclopropane who have received nitrous oxide in the

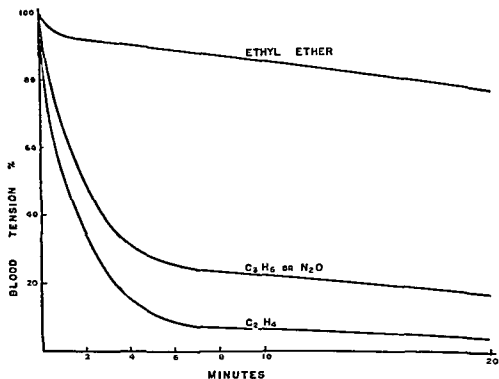


Fig 150—Elimination curves of anesthetics (Courtesy of Fink B R *Anesthesiology* 16 511 519, July, 1955 after Kety S S *ibid* 11 517, September 1950)

closing stages. The resultant anoxia may account for some of the excitement following cyclopropane anesthesia.

Diffusion anoxia and anoxemia may be important factors in the cyanosis of postpneumonectomy patients (reduced functional capacity, hence reduced mixing chamber) and in incidence of cardiac failure and arrest in patients with myocardial disease and may help to account for cardiac arrests occurring during intubation. Oxygen in high concentration should be administered for some minutes at conclusion of anesthesia and preceding interruption of anesthesia for procedures such as suctioning and laryngoscopy.



**Physiology of Respiration in Infants and Young Children.** Lung volume enlarges from 100 cc. at birth to 400 cc. at age 1, then more slowly. Chest circumference increases by 50% in the first 18 months. Differences in results obtained by different workers (Table 1) prompted J. E. Hall<sup>3</sup> (Hosp.

TABLE 1.—TIDAL VOLUME AND VITAL CAPACITY ACCORDING TO TWO WORKERS

AGE	PIECHAUD		FERRIS
	Tidal Volume, ML.	Vital Capacity, ML.	Vital Capacity, ML.
4	300	500	—
5	320	580	1,290
6	360	660	1,650
7	400	820	1,930
8	460	980	2,160
9	500	1,150	2,190
10	560	1,360	2,230
11	600	1,600	2,540
12	680	1,680	3,750
13	796	1,960	3,810

TABLE 2.—TIDAL VOLUME, RATE AND MINUTE VOLUME

AGE	TIDAL VOLUME, ML.	RATE PER MINUTE	MINUTE VOLUME, ML.
6 mo	64	55	3,500
1	79	45	3,700
1½	131	33	4,300
2	143	30	4,400
3	156	31	4,900
4	180	30	5,500
5	192	28	5,400
6	199	27	6,000
7	204	30	6,300
8	228	25	6,200

for Sick Children, London) to investigate respiration of children under anesthesia by spirometric tracings after various elective procedures. Increase in tidal volume parallels lung growth, respiratory rate falls with increasing age and hence minute volumes increase more gradually (Table 2). Because of the relatively fixed rib cage before age 2, increased respiratory needs can be met only by increasing rate. That increased CO<sub>2</sub> may be a reason for the high re-

spiratory rate in infants is borne out by results on dead space and tidal volume (Table 3), calculated by estimating dead space to be one fifth of tidal volume. Dividing actual area of trachea by lung volume for each age shows that relative dead space decreases with age, hence the need of high respiratory rates in infants. Dead space of anesthetic equipment added to dead space of child leaves inadequate effective tidal volume, resulting in only one-fifth normal alveolar ventilation up to age 1. The potential danger of

TABLE 3—TIDAL VOLUME AND DEAD SPACE

AGE	TIDAL VOLUME ML	DEAD SPACE ML
6 mo	64	12
1	79	16
1½	131	26
2	143	29
3	156	31
4	180	36
5	192	38
6	199	40
7	204	42
8	228	46

CO<sub>2</sub> retention can be avoided if flow rate of gases is sufficiently high in a semiclosed system.

► [A high flow rate of gases in a semiclosed system will prevent carbon dioxide retention only if it assists in washing out unnecessary equipment dead space. Carbon dioxide retention will develop in the presence of a high flow rate if alveolar ventilation is inadequate—Ed.]

Use of Pulmonary Function Tests with Special Reference to Anesthesia is described by Hurley L. Motley<sup>4</sup> (Univ. of Southern California). One group of measurements is of bellows action of chest and lungs and another is related to transport of O<sub>2</sub> and CO<sub>2</sub> to and from the blood. Total vital capacity, timed vital capacity for 3 seconds and maximal breathing capacity are obtained from rapid spirogram tracings (32 mm spread in 12 seconds) on the 135 L. Respirameter. A marked reduction of total vital capacity in standing, as compared to supine position, indicates severe pulmonary insufficiency. Timed vital capacity for 3 seconds is normally the same as predicted total vital capacity. Normal maximal breathing capacity indicates good function of

the diaphragm and good lung elasticity, without significant bronchospasm. The degree of bronchospasm is assessed quantitatively by comparing maximal breathing capacity before and immediately after a bronchodilator treatment. A slow prolonged exhalation curve on the spirogram indicates obstructed air flow, and failure of exhalation curve to return to beginning level indicates air trapping. Measurements from serial spirometers are useful in evaluating response to treatment, following a clinical course, screening tests for surgery or evaluating anesthetic risks.

The ratio of residual air to total lung capacity permits reliable evaluation of the degree of emphysema. If residual air occupies 35-45% of total lung capacity, emphysema is moderate, if 45-55%, advanced or severe, and if above 55%, very severe. A ventilation factor (timed vital capacity maximal breathing capacity and residual lung capacity) as low as 25% of predicted normal indicates a poor anesthetic risk.

Blood gases are measured on the Van Slyke manometer and pH on a glass electrode meter. A drop in arterial blood  $O_2$  saturation of 5-10% or more below resting level with mild exercise (1 minute step up test on a 20 cm stool) indicates severe disability. Increase in exercise  $O_2$  saturation above the resting level indicates less disability than is implied by resting measurements. Exercise saturation tends to decrease in severe emphysema, and in pulmonary fibrosis without emphysema the drop is often marked.

Elevated arterial  $CO_2$  indicates the possibility of development of respiratory acidosis during infection or with the use of sedatives, anesthetic agents or high oxygen breathing. Arterial blood pH is the best single measurement revealing exact status of the acid base balance and the presence of acidosis or alkalosis. The presence of drowsiness, stupor or coma in respiratory acidosis appears to be related to pH changes rather than absolute level of  $CO_2$  content or tension.

Concentration of carbonic acid in arterial blood can be rapidly reversed by increased elimination of  $CO_2$  from the lungs by hyperventilation which lowers alveolar  $CO_2$  tension and in turn blood  $P_{CO_2}$ . An abnormal quantity of fixed acid results in higher arterial carbonic acid and reflexively increases pulmonary ventilation. This decreases arterial

carbonic acid by blowing off  $\text{CO}_2$  and tends to restore the normal ratio more rapidly than kidneys do by acid excretion

In the postoperative phase, arterial blood oxygen may be satisfactory from  $\text{O}_2$  given by catheter, mask or tent, but decreased ventilation may result in inadequate elimination of  $\text{CO}_2$  and acidosis unless mechanical respiratory assistance is provided, e.g., with the Halliburton, Bennett or Emerson Units. Use of 60% helium and 40% oxygen with pressure breathing and bronchodilators is sometimes helpful in facilitating transfer of oxygen around secretions and in relieving bronchospasm. Use of helium with oxygen (not under 30%) is most helpful in severe emphysema with marked pulmonary infection, aggravated by bronchospasm.

**Oxygen Toxicity** Arterial and Internal Jugular Blood Gas Composition in Man during Inhalation of Air, 100%  $\text{O}_2$  and 2%  $\text{CO}_2$  at 3.5 Atmospheres Ambient Pressure was studied in four schizophrenic patients by C. J. Lambertsen, J. H. Ewing, R. H. Kough, R. Gould and M. W. Stroud, 3rd<sup>5</sup> (Univ. of Pennsylvania).

Changes in arterial and venous blood gases during air breathing at 3.5 atmospheres are smaller than, but qualitatively similar to, those produced by  $\text{O}_2$  breathing at the same pressure. Blood gas changes in both situations are consistent with previous studies of respiratory effects of air breathing at 3.5 atmospheres and effects of  $\text{O}_2$  breathing at 3.0 and 3.5 atmospheres on respiration, blood gas transport and cerebral circulation. These data suggest that increasing  $\text{P}_{\text{O}_2}$  of inspired air leads first to cerebral venous hypercapnia (by interference with  $\text{CO}_2$  transport), which in turn (through rise in  $\text{P}_{\text{CO}_2}$  in respiratory centers) causes hyperventilation, arterial hypocapnia and increased cerebral vascular resistance. This is in harmony with observed increases in cerebral arteriovenous  $\text{P}_{\text{CO}_2}$  difference from 8 mm Hg during air breathing at sea level to 13 mm Hg on  $\text{O}_2$  inhalation at the increased pressure. Corresponding increases in cerebral arteriovenous  $\text{O}_2$  tension difference were from 51 mm Hg at sea level to 146 (air breathing) and 1,824 mm Hg ( $\text{O}_2$  inhalation) at 3.5 atmospheres. Relative stability of cerebral venous  $\text{P}_{\text{O}_2}$  (38–44 and 76 mm Hg) probably

(5) J Appl Physiol 8:255–263 November, 1955

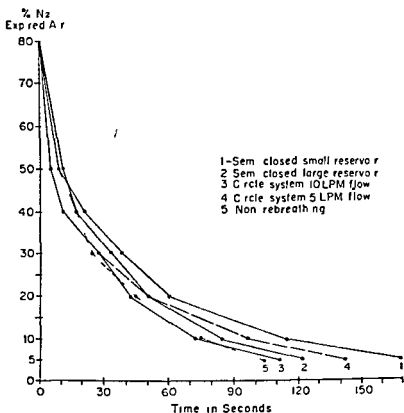


Fig. 151—Average denitrogenization curves of various systems tested (Courtesy of Hamilton W. K. and Eastwood D. W. *Anesthesiology* 16:861-867 November 1955)

gives 10% nitrogen in expired air. One breath of room air or a leak in the mask decreases the oxygen tension in the inspired gases and may reverse the gradient of nitrous oxide tensions between blood and alveoli.

**Factors Influencing Elimination of Nitrogen Using Semi-closed Inhalers** were studied in healthy volunteers by George G. Miles, Nicholas T. Martin and John Adrian<sup>8</sup> (Louisiana State Univ.). At flow rates equal to minute volume exchange of the subject, with no rebreathing, elimination occurred at an average of  $2\frac{1}{2}$  minutes. When flow rates lower than minute volume exchange were used, rebreathing became necessary, and elimination was prolonged in proportion to reduction in flow rate. After nitrogen was completely washed out by oxygen and the subject breathed room air, refilling time equaled desaturation time. With alveoli and plasma relatively free of nitrogen, and using a closed circle system with rebreathing and metabolic flow of

oxygen, excretion of tissue nitrogen was slow, requiring 30 minutes or more to eliminate 0.5-0.6 L.

Size of the inhaler does not appreciably alter nitrogen elimination time. Elimination curves for the to-and-fro inhaler differed little from those of the circle filter. Rate of elimination of nitrogen from anesthesia appliances corresponds closely to figures for nitrogen elimination obtained in pulmonary function studies using apparatus differing in design from anesthesia apparatus.

Nitrogen elimination curves in patients anesthetized with ethylene corresponded closely to those obtained using oxygen in volunteers. With 80% ethylene and 20% oxygen mixtures, when flow rates less than the minute volume exchange are used, oxygen tension in the inhaler is reduced below the physiologic limit. If oxygen concentration is increased, ethylene tension is reduced below that necessary to induce and maintain anesthesia. These data suggest that initially high flow rates be used to eliminate nitrogen. The flow rate may then be reduced with an oxygen enriched mixture. Similarity between displacement of nitrogen by oxygen and ethylene oxygen mixtures suggests that this pattern applies to other gases such as helium and nitrous oxide.

**Anesthesia for Tonsillectomy in Children - Endotracheal Technique, with Cardiovascular Observations.** According to Vincent J. Collins and Alfred Granatelli<sup>9</sup> (St. Vincent's Hosp., New York), the most neglected of anesthetic procedures is that for tonsillectomy. It is relegated to the novice and conditions are permitted that would not be tolerated in an adult patient. From the moment the child is hospitalized, he is shocked psychologically, physiologically, and pharmacologically. A child undergoing tonsillectomy should have the best anesthetic technique possible rendered by the best anesthetist available.

Preoperative preparation is primarily psychological and includes a preoperative visit from the anesthesiologist who must gain the confidence of the child and explain the program of the following day. Recommended premedication is scopolamine, intramuscularly, and 50-150 mg secobarbital,<sup>\*</sup> rectally. The subsequent anesthetic inductions in the 50 cases reported, were all carried out with a vinyl ether-

(9) J. A. M. A. 161:59 May 5 1956

diethyl ether sequency by the open drop technic. Thereafter anesthesia was maintained with an ether-oxygen mixture. It was given after endotracheal intubation by the orotracheal route under direct laryngoscopy in 25 patients and by using the ether hook for insufflation in the other 25.

Comparison of the two groups revealed some disadvantages in both methods, but the drawbacks of the endotracheal technic are far outweighed by the advantages of (1) minimal disturbance of physiology, (2) no asphyxia, (3) good oxygenation and control of respiration, (4) ideal working conditions, i.e., quiet field, (5) unhurried surgery, (6) diminished bleeding, (7) control of secretions and (8) no aspiration of blood.

► [The authors have been liberal in their conclusions based on experience with only 50 patients. Although there is much to recommend the use of an endotracheal catheter as a part of the anesthetic technic for tonsillectomy, there are insufficient data in this article to support the conclusions. One wonders if the routine use of an endotracheal catheter is not on occasions a substitute for an inability to maintain an airway or for unwillingness to exert the effort necessary to maintain an airway without this artificial device—Ed.]

---

## MUSCLE RELAXANTS

**Facial Paralysis and Muscle-Relaxant Anesthesia** Paul M. Osmun<sup>1</sup> (Seattle) reports a case illustrating the insidious danger of using succinylcholine-drip, muscle-relaxant anesthesia in an operation in which identification of the seventh cranial nerve is important to its preservation.

Woman, 32, had mastoidectomy. As the bridge was being thinned what appeared to be a mastoid cell was uncovered 1 mm below the horizontal semicircular canal and 1 mm behind the crest of the facial ridge. When the cell or nerve was pressed, no muscle response occurred in the face. Because of relative elevation of the facial ridge this mastoid cell or nerve was uncovered to a length of about 2 mm. It was stimulated with the back of a curet four times, with no facial response. When the anesthetic was discontinued, she regained consciousness immediately. The face was totally paralyzed on the operated side. Since succinylcholine had been given in such quantity as to cause complete muscle relaxation stimulation by pressure on the facial nerve to identify the nerve was not a reliable procedure. On reexploration the next day the area was uncovered for 1.5 cm. There was no response in the face with use of a non muscle relaxant.

(1) A M A Arch Otolaryng 63:529, May 1956

anesthesia. The facial nerve was grossly swollen and injected. A small black linear streak was noted in the horizontal canal. Pressure against the area of the stapes caused bubbles to emerge from the fistula.

► [The employment of routine anesthesia (and nitrous oxide-succinylcholine drip seems to be a currently popular routine) tends to diminish the awareness of the value of individual patients' problems.—Ed.]

**Relaxant Action in Man: Experimental Study; II. Results with Intravenous Gallamine Triethiodide** are reported by William W. Mapleson and William W. Mushin<sup>2</sup> (Welsh Nat'l School of Medicine).

**METHOD.**—Submaximal electric stimuli, consisting of 1.2 second bursts of 50/second square current pulses repeated at 6 second intervals, are applied to the median nerve at the wrist by a multiwick surface electrode to develop tension in short muscles of the thumb. The amount by which tension, at any time after intravenous injection of gallamine, falls short of normal preinjection tension, when expressed as percentage of normal, gives percentage depression of muscle response. Theoretically, this is a valid measure of degree of relaxation (percentage of fibers in muscle which fail to contract in response to stimuli of a given frequency arriving from its motor nerve) at the stimulus frequency.

Sixteen of 18 usable recordings (12 on one subject, A.A.) showed a characteristic rapid increase of relaxation toward a peak, followed by a slower return to normal. Eight of 11 recordings on subject A.A. coincided closely over the region from shortly after the peak to about 15% relaxation. Three showed a relatively slower return to normal. That five recordings in one subject were consistent and another three nearly so (Fig. 152) supports the reliability of the method in general and the accuracy of determining degree of relaxation in stimulated muscle, in particular. Information derived from practically all of a recording was used to check the shape of the dose-effect curve, by Teorell's equation. When this equation was fitted to results of five recordings forming the main series on A.A., making use of normal sigmoid dose-effect curve, the difference between observed and theoretic effect never exceeded 1.5% relaxation except for the first 1½ minutes, where the theoretic effect always fell short of observed effect, sometimes as much as 12%. Relation between peak effect and logarithm dose can be faithfully represented by a normal sigmoid curve, at least to about 60 or 70% relaxation. The equation was then used to predict theoretic effect-time curves for doses of galla-

(2) *Anaesthesia* 10:379-390, October, 1955.



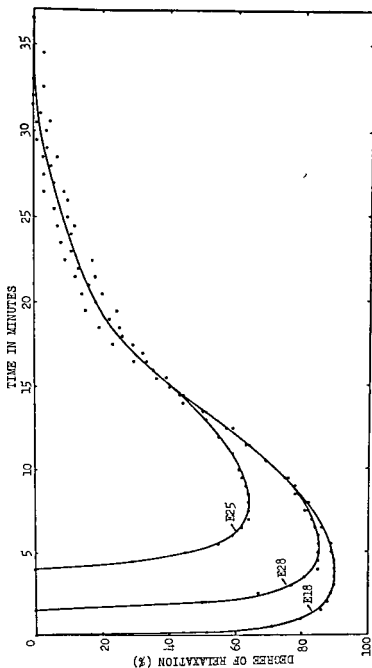


Fig 152—The three observed effect time curves of subject A A that show a slow return to normal following gallamine intravenously (Courtesy of Mapleson, W W, and Mushin, W W Anaesthesia 10 379 390, Octo ber, 1955 )

mine larger than those considered safe in these experiments

Degree of relaxation of only one small group of muscles was measured Ptosis, as estimated by the subject, appeared roughly equal to the measured relaxation of thumb muscles Conversely, diplopia was noticed with doses of gallamine too small to produce any measured relaxation

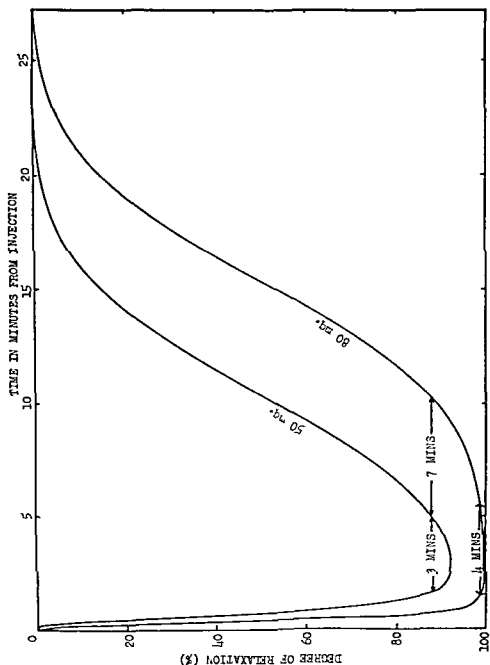


Fig. 153 --Theoretic effect time curves for intravenous injections of 50 and 80 mg gallamine in a 70 kg subject (similar to subject A A) (Determined by use of Leorell's equation) (Courtesy of Mapleson, W. W., and Nishin, W. W. *Anaesthesia* 10 379 390, October, 1955)

Dropping of the jaw and a sensation of "lump in the throat" became noticeable only at measured relaxations of 45-65% in one subject and 75-90% in another. Respiratory insufficiency was never noted. Wide variation in response of various muscles to a given dose of gallamine is hypothetically explained as follows. The extent to which a moderate dose of relaxant impairs the ability of a muscle to

carry out some function depends on what fraction of its maximum power is involved in performing that function and, probably, on what range of frequencies is involved in its natural stimulation. Thus, a muscle that would normally be contracting nearly maximally (hence receiving natural stimuli at relatively high frequency) will suffer greater depression of activity than one which would normally be contracting only to a small extent.

Figure 153 indicates that clinical descriptions of duration of gallamine effect have little meaning unless degree of relaxation is stated. The 20-25 minute duration often quoted must be related to time taken for return to normal following a dose of 80 mg. in an average adult, according to the authors' results and findings of others, but can be of little clinical interest since lesser degrees of relaxation have little clinical utility.

From Teorell's theory, the effect of "topping up" doses both in time and magnitude, would be reproducible and unchanged over prolonged periods, assuming that circulation through muscles and excretory efficiency remain constant. During major operations, however, progressive depression of circulation and of excretion may cause gradual prolongation of time for reappearance of signs of inadequate relaxation after each dose, and therefore would require gradual prolongation of time between each necessary topping up dose.

---

## BARBITURATES

Comparative Clinical and Statistical Study of Thiopental and Thiamylal in Human Anesthesia is reported by Ralph M. Tovell, Charles C. Anderson, M.D.,<sup>1</sup> M. J. Love, Joseph F. Artusio, Jr., E. M. Papper, Charles J. Wiley, Fernando Hudon, Scott A. Smith and George S.<sup>2</sup> The blind study involved thiopental and thiamylal routine

or recovery time. Statistically significant differences between the two drugs, probably of no clinical importance were (1) greater duration of laryngospasm with thiamylal (2) greater elevation of blood pressure during the maintenance period for thiamylal (3) higher incidence of dizziness in the recovery period with thiamylal and (4) larger amount of thiopental when expressed as total amount of drug necessary to accomplish the endpoint of "intubation". This last difference disappeared when the amount of thiopental per pound and amount/pound/minute were determined. No significant difference appeared in other endpoints selected for the induction period. No apparent differences of clinical significance have been observed between thiopental and thiamylal in human subjects.

► [This is a classic example of the excellent manner in which the clinical application of drugs can be accurately appraised. The reader should compare the evidence presented in this study with the advantages of one of these drugs over the other reported by enthusiastic and biased observers whose data consisted of clinical impressions and guesses—Ed.]

**Comparison of Electroencephalographic Patterns during Steroid and Barbiturate Narcosis** J. Weldon Bellville, William S. Howland and C. Paul Boyer<sup>4</sup> (Cornell Univ.) compared EEG patterns obtained with viadril, pentobarbitone, thiamylal and hexobarbitone in 36 patients undergoing relatively minor surgical procedures. No characteristic changes could be attributed to any one agent, but at deeper levels pentobarbitone EEG's could be distinguished since return from pattern 4 or 5 to pattern 2 was much slower than with other drugs studied.

The first change from the awake pattern is an increase in frequency to 20-30 c/second. There may be slight increase in amplitude. The patient at this time is drowsy. As the amount of drug is increased the pattern becomes of greater amplitude (to 200  $\mu$ v) and spiky. The frequency is compound and consists of 20 cycle activity superimposed on slower 8-12 cycle activity. The third level is characterized by silent areas or periods of "burst suppression" lasting one to three seconds. Areas of activity or "bursts" are composed of mixed frequencies, mainly 6-10 c/second with superimposed low voltage fast waves. By increasing the amount of agent level 4 may be obtained, this has burst suppression of 3-10 seconds duration. Patients with this

(4) Brit. J. Anaesth. 28:50-54, February 1956

carry out some function depends on what fraction of its maximum power is involved in performing that function and, probably, on what range of frequencies is involved in its natural stimulation. Thus, a muscle that would normally be contracting nearly maximally (hence receiving natural stimuli at relatively high frequency) will suffer greater depression of activity than one which would normally be contracting only to a small extent.

Figure 153 indicates that clinical descriptions of duration of gallamine effect have little meaning unless degree of relaxation is stated. The 20-25 minute duration often quoted must be related to time taken for return to normal following a dose of 80 mg. in an average adult, according to the authors' results and findings of others, but can be of little clinical interest since lesser degrees of relaxation have little clinical utility.

From Teorell's theory, the effect of "topping up" doses both in time and magnitude, would be reproducible and unchanged over prolonged periods, assuming that circulation through muscles and excretory efficiency remain constant. During major operations, however, progressive depression of circulation and of excretion may cause gradual prolongation of time for reappearance of signs of inadequate relaxation after each dose, and therefore would require gradual prolongation of time between each necessary topping up dose.

---

## BARBITURATES

Comparative Clinical and Statistical Study of Thiopental and Thiamylal in Human Anesthesia is reported by Ralph M. Tovell, Charles C. Anderson, Max S. Sadove, Joseph F. Artusio, Jr., E. M. Papper, Charles S. Coakley, Fernando Hudon, Scott M. Smith and George J. Thomas.<sup>3</sup> The blind study involved 1,098 thiopental and 1,245 thiamylal routine clinical anesthetics.

There was no statistically significant difference between thiopental and thiamylal with regard to potency, cardio-toxicity, respiratory depression, incidence of laryngospasm.

or recovery time. Statistically significant differences between the two drugs, probably of no clinical importance were (1) greater duration of laryngospasm with thiamylal (2) greater elevation of blood pressure during the maintenance period for thiamylal (3) higher incidence of dizziness in the recovery period with thiamylal and (4) larger amount of thiopental, when expressed as total amount of drug necessary to accomplish the endpoint of "intubation". This last difference disappeared when the amount of thiopental per pound and amount/pound/minute were determined. No significant difference appeared in other endpoints selected for the induction period. No apparent differences of clinical significance have been observed between thiopental and thiamylal in human subjects.

► [This is a classic example of the excellent manner in which the clinical application of drugs can be accurately appraised. The reader should compare the evidence presented in this study with the advantages of one of these drugs over the other reported by enthusiastic and biased observers whose data consisted of clinical impressions and guesses—Ed.]

**Comparison of Electroencephalographic Patterns during Steroid and Barbiturate Narcosis.** J. Weldon Bellville, William S. Howland and C. Paul Boyan<sup>4</sup> (Cornell Univ.) compared EEG patterns obtained with viadril, pentobarbitone, thiamylal and hexobarbitone in 36 patients undergoing relatively minor surgical procedures. No characteristic changes could be attributed to any one agent, but at deeper levels pentobarbitone EEG's could be distinguished since return from pattern 4 or 5 to pattern 2 was much slower than with other drugs studied.

The first change from the awake pattern is an increase in frequency to 20-30 c/second. There may be slight increase in amplitude. The patient at this time is drowsy. As the amount of drug is increased the pattern becomes of greater amplitude (to 200  $\mu$ v) and spiky. The frequency is compound and consists of 20 cycle activity superimposed on slower 8-12 cycle activity. The third level is characterized by silent areas or periods of "burst suppression" lasting one to three seconds. Areas of activity or "bursts" are composed of mixed frequencies, mainly 6-10 c/second with superimposed low voltage fast waves. By increasing the amount of agent level 4 may be obtained, this has 'burst suppression' of 3-10 seconds duration. Patients with this

degree of cortical depression will move on surgical stimulation unless nitrous oxide is added to inhaled oxygen. Level 5 is arbitrarily assigned to the EEG pattern seen when duration of cortical suppression persists 10 seconds or longer.

More detailed and precise studies of EEG changes during anesthesia are necessary if the EEG is to be of aid in understanding mechanisms involved in anesthesia and narcosis. Important changes in EEG activity may escape interpretation that could be detected by EEG frequency spectrum analysis correlated with plasma oxygen, carbon dioxide and anesthetic concentration.

► [One should not assume that because the electroencephalographic tracings are similar either of these drugs or neither of them produced a narcotic or anesthetic state.—Ed.]

**Observations on Convulsive and Subconvulsive Electrotherapy during Intravenous Anesthesia.** Clarence W. Olsen<sup>5</sup> (Beverly Hills, Calif.) emphasizes certain possibilities of the use of available electric equipment in respiratory emergencies. However, the established requirements of anesthetic technic must always be kept in mind.

Reflex spasm, closing the larynx and obstructing respiration, can be avoided to some extent by preliminary injection of atropine. After incipient development of this complication, oxygen may cause relaxation of the spasm; but, when one is prepared to administer electric convulsion therapy, it seems best to proceed with the treatment. An electrically induced convulsion, lasting about 30-45 seconds, suffices to eliminate obstruction due to laryngospasm by temporarily deepening the anesthesia. This is a recommended but relatively hazardous method, unless it is preparatory to laryngeal intubation and positive pressure respiration. However, the short time consumed in the usual grand mal response to electric stimulation does not seem to aggravate the situation seriously. Routine use of a relaxant, flaxedil,<sup>6</sup> may contribute to avoidance of serious and persistent laryngeal spasm.

Pharyngeal obstruction due to flaccidity and swelling of the tongue is easily remedied by introduction of an artificial self-retaining airway. It can be more simply prevented or relieved by lifting the jaw forward, or having the patient

(5) *Dis. Nerv. System* 17:169-171, May, 1956.

lie in the semiprone position rather than flat on the back after treatment.

Apnea due to rapid injection of barbiturate presents little difficulty if electric stimulation is administered almost immediately. Either convulsive or subconvulsive stimulation is usually effective. Occasionally apnea is prolonged after a convulsive response; here the minimal electric stimulation first suggested by Robie finds application. Olsen uses controlled alternating current and leaves the electrodes in place after convulsive treatment until spontaneous respiratory movements are observed. If apnea persists more than 10 seconds after the last clonic movements have subsided, application of a current rising from zero and reaching 25-50 ma. in a second, then returning to zero, and applied at intervals of 5 seconds, results in a gentle shudder, followed by a gasp, at each application. The current is applied bitemporally, simply because the electrodes are already at the temples. However, Robie's technic of electric stimulation for barbiturate poisoning presumes bitemporal placement of electrodes, on the assumption that cortical and diencephalic stimulation is desirable.

► [It seems heroic if not unphysiologic to increase oxygen demand and carbon dioxide production in a state of inadequate respiratory exchange by the induction of severe muscle activity. One wonders also if there is any more specificity to the restoration of ventilation by the current employed than there is to the pain of a needle stick.—Ed.]

**Shivering Following Thiopental Sodium and Other Anesthetic Agents.** Robert M. Smith, Leonard Bachman and Tiina Bougas<sup>6</sup> (Children's Med. Center, Boston) evaluated incidence and significance of shivering after thiopental, ether and cyclopropane anesthesia in 259 children. Special precautions were taken to exclude pyrogens. Air conditioned operating rooms were used. Postanesthetic tremors occurred in 65% of 120 patients given pentothal,<sup>\*</sup> 31.7% of 120 patients given ether and 25% of 20 patients given cyclopropane. Tremor simulated true thermal shivering in every way and occurred only in a light plane of anesthesia.

Arterial CO<sub>2</sub> and pH measurements in seven patients before termination of pentothal<sup>\*</sup> anesthesia gave no evidence that shivering was related to CO<sub>2</sub> excess or hypocarbica. In three instances, EEG did not demonstrate in-

(6) *Anesthesiology* 16:655-664, September, 1955.



creased cortical irritability during or after pentothal<sup>8</sup>. Central and surface temperature changes under thiopental did not suggest any significant depression of temperature-regulating mechanisms. Increased sensitivity to cold following thiopental N<sub>2</sub>O-O<sub>2</sub> anesthesia was suggested by observation of shivering in warmer rooms and with less heat loss than after ether or cyclopropane. Large ventilatory heat loss, early awakening and rapid return of shivering reflex seem to play contributing roles in thiopental shivering. This drug may lower heat production through depression of adrenal activity and glycogen metabolism, though shivering does not occur with spinal anesthesia associated with adrenal blockade.

Regardless of cause, shivering may be harmful because increased oxygen demand may be dangerous to a patient with poor cardiorespiratory reserve.

---

## SPINAL ANESTHESIA

**Long Term Follow-up of 10,098 Spinal Anesthetics: II. Incidence and Analysis of Minor Sensory Neurologic Defects.** In a study of the 8,460 patients given spinal anesthetics, Leroy D. Vandam and Robert D. Dripps<sup>7</sup> (Hosp. of the Univ. of Pennsylvania) noted residual signs or symptoms of numbness, restricted in most to the lumbar and sacral areas, in 71 patients (0.8%). None of the 71 had other neurologic signs, the disease was not progressive and most complaints disappeared within six months. Accurate information was obtained for 86% of the anesthetics for at least six months after anesthesia, and a parallel study was conducted in 1,000 patients given general anesthesia for the same type operations.

Complaints of cramps, twisting, etc., termed irritative symptoms, subsiding in the first few days after surgery, occurred in 1% of the patients given spinal anesthetics. As they also occurred in 0.9% of the patients given general anesthetics, they are not included in the report. Numbness in toes and feet occurred in 6 patients, with no objective neurologic signs; perineal numbness in 6, 2 with objective

(7) Surgery 38 463 469, September, 1955

signs, leg numbness with and without pain in 20, none with objective signs, numbness without pain in thighs in 20, 6 with objective evidence, numbness with pain in thigh in 19, with sensory loss in 7 of 12. The last symptom complex was identical with "meralgia paresthetica," a disease affecting the lateral femoral cutaneous nerve which is anatomically very liable to peripheral trauma. Factors in spinal anesthesia leading to this disturbance have not been elucidated.

Analysis of the above data suggests that the spinal anesthetic injected was implicated in the succeeding difficulties, albeit as a nonspecific factor. Errors in technic administration—e.g., traumatic puncture, paresthesia at time of lumbar puncture or the operation itself—surgery in close proximity to the area of later numbness or mechanical factors associated with the operation—such as positioning of the legs in stirrups—could not be implicated. Complaints reported were of minor significance. There were no cases of the cauda equina syndrome, myelitis or meningitis.

**Spinal Anesthesia Survey of Neurologic Complications.** Hall G. Holder and Clifford L. Graves<sup>8</sup> (San Diego) reviewed 32,822 completed records of patients who had received spinal anesthesia. Of 500 questionnaires sent to practicing physicians, the 370 returned showed that 16 patients had had neurologic complications, an incidence of 0.049%. Of the 16, 11 had had transient motor sensory disturbances from which they had fully recovered within six months, 3 had persistent motor or sensory disturbances, 1 had had progressive adhesive arachnoiditis with fatal outcome and 1 had had abducens paralysis with complete recovery within six months. Hence the incidence of severe neurologic complications was 1 in 10,000 (0.012%).

In one patient, the complication may have been due to the underlying pathology of intravertebral disk. Two patients with hemorrhoidectomy had symptoms in the external femoral cutaneous nerve, which has been reported after general anesthesia, presumably due to local pressure.

Critical evaluation of the data and reports in the literature suggest that errors in technic, such as inaccurate or traumatic introduction of the needle, contaminated spinal puncture, either bacterial or chemical, errors in technic of administration of the drug or undiagnosed pre-existing disease

(8) California Med. 82:426-429 June 1955

of the spinal cord may be responsible for the complications. Scrupulous technic and care in sterilizing ampules should be exercised. Chances of trauma and toxic concentrations of the drug are much more likely to occur in continuous spinal anesthetics. There is no evidence that toxic drug concentrations occur in single dose spinal anesthetics. Morbidity associated with spinal anesthesia compares favorably with that associated with general anesthesia.

► [The preceding two articles in which exhaustive investigation has been made of the sequelae of spinal anesthesia should serve to de-emphasize the hysteria associated with this highly acceptable anesthetic technic in respect to neurologic sequelae. It is important to realize however, as pointed out in both of these articles that utmost care must be paid to every detail in technic, carelessness, inattention and lackadaisical attitudes are associated with significant increase in undesirable results. The evidence in these articles is convincing especially in the first, in which the observations are limited to one institution.—Ed.]

**Adhesive Arachnoiditis and Vascular Blockage Caused by Detergents and Other Chemical Irritants. Experimental Study by E. Weston Hurst<sup>9</sup>** (Manchester, England) was undertaken because detergents contaminating material injected to produce spinal anesthesia have been blamed for ensuing neuropathy. Monkeys were used as experimental animals, and a great variety of detergents and other chemical substances were tested.

A number of diverse substances, when introduced into spinal fluid in appropriate concentration, caused lesions that may be classified as follows: (1) Variable superficial damage to areas of nervous tissue immediately beneath the pia or in the 4th ventricle, in close contact with the irritant. Nerve roots are erratically involved, and there is chromatolysis of a few cells of the anterior horns. If the irritant were given into the lumbar theca corresponding lesions would be peripheral degeneration of the spinal cord, degeneration of some nerve roots, ascending degeneration of posterior columns, etc., precisely the lesions commonly mentioned as following spinal anesthesia in animals or in man. (2) Cellular proliferation accompanied by inflammatory exudate in the meninges. When sufficiently intense, this impedes flow of cerebrospinal fluid sufficiently to lead to fatal internal hydrocephalus. Adhesive arachnoiditis or fibrotic changes in meninges have been recorded in man or animals given spinal anesthetics. (3) Necrosis of media and

(9) *J. Path. & Bact.* 70:167-178, July 1955.

perhaps also of adventitia of meningeal vessels, which then react variously, tending toward obliteration of the lumen and restriction of blood supply to nervous tissues. End results of this lesion have recently been clearly recognized as following spinal anesthesia in man.

The attribution of sequelae of spinal anesthesia to accidental contamination of the anesthetic with detergents disregards the fact that clinically similar accidents were apparently occurring before modern detergents were in common usage. The present work shows that, in suitable concentration, detergents can be responsible, though a single attempt to contaminate a syringe to mimic conditions in hospital practice did not give a positive result. On available evidence, anesthetic agents themselves cannot be dismissed as possible causes of sequelae of spinal anesthesia, and a reappraisal in the experimental animal of toxic effects of these substances would appear to be urgently needed.

There was no evidence that sensitization played a role in the lesions produced, findings indicated only direct irritant action of the chemicals tested and were different from those evoked by anti-brain serums, which presumably involve an antigen-antibody response.

**Pathology of Paraplegia Occurring as a Delayed Sequela of Spinal Anesthesia, with Special Reference to Vascular Changes.** J. G. Greenfield, A. G. Rickards and G. B. Manning<sup>1</sup> (London) report autopsy findings in the nervous system in three women, aged 46, 37 and 40, whose deaths followed spinal anesthesia within 9 weeks to 6 months. In all, the pia arachnoid was considerably thickened, and this appeared to be the cause of hydrocephalus and optic atrophy in the third case. In the other two, paraplegia came on very rapidly and appeared to be due chiefly to a vascular lesion of unusual type, this lesion was found also in the first case. Operations were carried out in the same operating theater, although the anesthetic was administered by different anesthesiologists.

The lesions in the meningeal vessels, over lower thoracic and lumbosacral segments of the spinal cord, consisted in a replacement of the muscular coat of the media by collagen, stretching and breakage or reactionary thickening or reduplication of the elastica and thickening of the intima. The

(1) *J. Path. & Bact.* 69:95-107, Jan-Apr, 1955.

last was usually concentric and appeared to be related to lesions of other coats

Correlation of clinical and pathological findings indicates the probable course of the pathogenic process. Some irritant introduced into the lumbar culdesac caused progressive thickening of the pia arachnoid and damaged the media of meningeal vessels. The elastica probably also was damaged in some arteries, causing it to react by thickening or reduplication. In other arteries the elastica appeared merely stretched. Damage to the intima may have been primary or secondary, probably in most cases it was due to dilatation of the vessel because of the medial lesion. The outer zone of acellular fibrous tissue under the elastica seen in some vessels might have been caused by toxic action on the intima. Only one vessel showed thrombosis. Lesions in white columns of the spinal cord in two cases were evidently related to the arterial lesions. The severe narrowing of small meningeal arteries in the first case agreed with the clinical history of rapid onset of paraplegia nearly two months after spinal anesthesia. Probably the intimal thickening was a slowly progressive process, probably secondary to more acute damage to the media, which followed at a much shorter interval. Evidence of inflammatory reaction in vascular walls was very slight, and only one small vessel had undergone total necrosis.

The nature of the irritant or toxic substance introduced by lumbar puncture and its mode of action remain undecided. Either the anesthetic itself or some contaminant introduced with it may have been at fault and may have produced lesions either by a direct toxic or by an indirect hyperallergic action.

**Nerve Complications of Spinal Anesthesia** Three Cases of Spinal Syndrome after Injection, with Areflexive Paralysis of a Lower Extremity, Partially Dissociated Sensory Disturbances and Late Osteoarticular Trophic Disturbances. In two of the cases reported by L. Barraquer Ferre and L. Barraquer Bordas<sup>2</sup> (Barcelona, Spain), the first discomfort radiating to the leg was felt at the moment of puncture (not after injection of the anesthetic). The needle was withdrawn and reinserted. The third patient noticed nothing until the anesthetic solution was injected.

(2) *Acta neurol. et psych. belg.* 56:177-187, March 1956.

Clinically, the syndrome in the three patients was remarkably uniform, consisting of flaccid paralysis or paresis of a lower extremity, with deep muscular areflexia, predominantly distal, and uniform or predominantly distal disturbance of sensation in the leg, involving principally pain and thermal sense and, to a lesser degree, tactile and vibratory sensation. Kinetic sense was normal.

In Case 1, in which evolution of the syndrome was followed from the beginning, sensory disturbance at first reached the 8th dorsal dermatome (but receded slightly afterward) and terminated definitely at the midline. Sensory integrity of the lowest dermatomes, apart from the 2d sacral, remained intact. The patients in Cases 2 and 3 were not examined until the syndrome had regressed. In Case 2, sensory deficiency increased in the last dermatomes and scars from burns testified to past sensory lack. In Case 3, there was frank diminution of sensation in the distal region of the foot, approximately in the region of the 1st sacral. Patellar and achilles reflexes of the affected extremity were abolished but were normal on the other side. Plantar cutaneous reflexes could not be obtained. In all three, cutaneous abdominal reflexes were abolished or doubtful on the affected side, and in Case 1 abdominal muscular reflexes were absent. Transitory disturbance of sphincters, with retention, lasted only a few hours in Cases 1 and 2. In Case 3, a peritoneal complication prevented evaluation. Electrodiagnosis of parietic muscles in Case 1 showed absence of qualitative changes.

Osteoarticular trophic disturbances were particularly striking in Case 2, causing significant pathologic changes in the knee. An x-ray showed a lateral subluxation, with longitudinal rotation of the axis of the femur with respect to that of the tibia, partial recession of the tibial plane, presence of osseous neoformations, probably due to periostitic reaction, and zones of osteosclerosis. In Case 1, less than two years after onset of the nerve lesion, significant shortening of the great toe (presumably from neurodystrophic osteolysis) was present on the affected side. In Case 3, no osteoarticular dystrophy was evident at a single examination.

Slow and incomplete regression (except for osteoarticular trophic changes) differentiates these lesions from arach-

noiditis or other more extensive, adhesive progressive meningiopathies. Topographic distribution of lesions indicates actual traumatism of the spinal cord.

**Paraplegia Following Spinal Anesthesia.** In a case reported by J. P. Payne (London) and S. E. Bergentz<sup>3</sup> (Falun, Sweden), the anesthetic itself is incriminated.

Woman, 45, in the fall of 1954 had laparotomy for relief from intestinal obstruction. She was placed in the lateral position, and spinal anesthetic was given by the surgeon. The spinal needle and syringes were autoclaved, and the skin was prepared with a 70% solution of ethyl alcohol. A 1:500 "light" solution of cinchocaine hydrochloride (nupercaine®) was used (20 ml.), and before the neck of the ampule was opened, it was sterilized with 70% alcohol; at no time was it immersed in antiseptic. Postoperative course was uneventful until the seventh day, when she had slight weakness in the right leg. After discharge, this became more pronounced, and by December 1954, she was unable to walk unaided. There was progressive deterioration, with spread of weakness to the left leg. For three weeks before hospitalization in February 1955, she was unable to walk, bladder control had become more difficult and constipation increasingly troublesome.

Provisional neurologic diagnosis was spinal tumor. At laminectomy, a cystic swelling extending upward at the level of the sixth thoracic vertebra was seen compressing the cord and apparently was continuous with the subarachnoid space. Postoperatively, the condition improved for two weeks but then regressed to the preoperative state. Histologic examination showed adhesive arachnoiditis. There was no evidence of spinal tumor.

Numerous cases of adhesive arachnoiditis have been reported following light cinchocaine anesthesia. The most likely explanation for the increased risk with this anesthesia is related to the volume used. When 10-20 ml. of anesthesia solution is injected into the spinal theca, there is considerable risk of displacement of cerebrospinal fluid, so that membranes and cord, particularly in the immediate vicinity of injection, are bathed in a solution which remains relatively undiluted. Adhesive arachnoiditis is particularly likely to develop in patients who receive continuous spinal anesthesia, in which a limited area of spinal cord and meninges tends to be in prolonged contact with the potentially noxious solution.

Though much work remains to be done on adhesive arachnoiditis, sufficient evidence exists to justify abandoning techniques that require large volumes or continuous injection of anesthetic solution. Permanent paraplegia, with its pro-

(3) *Lancet* 1 666-668, May 12, 1956.

found social and economic repercussions, is too great a price to pay for any temporary advantage gained by the surgeon

► {The preceding five articles present complications of spinal anesthesia. The inclusion of these articles is not an attempt to refute the evidence presented in the first two abstracts. They do serve to emphasize the necessity for meticulous attention to technique. For example, note the influence of minute amounts of detergent introduced intrathecally (wet sterilization of ampules is being almost universally abandoned). Note also the possibility of trauma as a factor in the production of neurologic sequelae. One can seriously doubt the incrimination of long acting agents as suggested in the last article, since other factors may have been responsible for the histologic changes—I d }

**Successful Treatment of Postlumbar Puncture Headaches** is reported by W E Murry, R B Busch, Jr, and J S Denson<sup>4</sup> (Los Angeles). Complete relief of headache was secured in 173 (71.2%) of 243 patients who received either caudal or epidural blocks with saline. Of these, 19 required a second block the following day for permanent relief. "Almost complete" relief was obtained by 31 patients (12.7%), who tolerated an erect position without difficulty. Headache was still present, but tolerable, in 26 (10.7%). Only 13 patients (5.3%) reported no relief. Nuchal stiffness or soreness was unrelieved in any case in which it was present, though the typical headache was completely eradicated. Volume of saline solution injected varied from 10 to 120 cc, most patients receiving 30-50 cc. There were no associated complications with this procedure. The caudal approach is preferred to the lumbar epidural route because technically there is less likelihood of repuncturing the dura.

**Effect of Hypotension Due to Spinal Anesthesia on Coronary Blood Flow and Myocardial Metabolism in Man** was studied in 12 patients by Donald B Hackel, S M Sancetta and Jerome Kleiner<sup>5</sup> (Western Reserve Univ.).

**METHOD**—The coronary sinus was catheterized and coronary blood flow, myocardial oxygen, glucose, lactate and pyruvate consumption were determined. Coronary vascular resistance was calculated by dividing mean arterial blood pressure by coronary blood flow (ml/100 Gm myocardium/second). The myocardial extraction coefficient for oxygen was determined as the quotient of coronary arteriovenous difference for oxygen divided by the arterial level. This expresses the per cent oxygen extracted by the myocardium from a unit of blood. These determinations were made in six patients, followed by induction of spinal anesthesia. In four, level of anesthesia was high; in two, low. In all, significant fall in arterial blood pressure occurred. A second set of determinations was done a half

(4) *Am J Surg* 91:394-395, March, 1956

(5) *Circulation* 13:92-97, January, 1956



hour after induction of spinal anesthesia. The other six patients served as double controls, without anesthesia, to determine variations a half hour apart in absence of hypotension and to indicate the change that occurred due to blood sampling and manipulative procedures. Before the study and for a week thereafter, 12 lead ECG's were taken.

In all patients given spinal anesthesia, coronary blood flow fell parallel with the decrease in mean arterial pressure. Mean coronary vascular resistance thus did not change significantly though individual cases varied greatly. The double controls showed random variations in blood pressure and coronary blood flow. Despite markedly reduced coronary flow in six patients after spinal anesthesia, four showed increase in coronary sinus oxygen content and one only slight decrease. Thus, total oxygen consumption by the heart decreased in all five. The sixth showed marked reduction in coronary sinus oxygen content and slight increase in total myocardial oxygen consumption, but this patient did not exhibit a steady state, and results cannot be compared with those in the others. The controls showed only slight random variation in coronary arteriovenous oxygen differences and in total myocardial oxygen utilization.

The essential hypertension present in four of six patients given spinal anesthesia permits comparison between pre-anesthetic values in hypertensive and normotensive patients. Coronary flow and left ventricular oxygen utilization appear to have been greater in the former. Myocardial glucose, lactate and pyruvate extraction showed only slight random variation with spinal anesthesia and in the double controls. These observations indicate a distinct difference between hypotension due to spinal anesthesia, with no conclusive metabolic effect on the heart, and experimental hemorrhagic shock which produced very small or negative myocardial pyruvate extraction and high arterial concentrations of lactate, glucose and pyruvate.

In no instance were ECG changes suggestive of myocardial hypoxia except in one patient with subendocardial ischemia that followed sudden blood pressure drop, with reversion to normal in less than 24 hours. In one patient, peripheral vascular collapse and subendocardial ischemia were precipitated by removing 70 ml blood for postspinal observations. Evidently the high spinal anesthesia had expanded vascular volume to a point where any further re-

duction of effective blood volume critically limited venous return to the heart. In addition, the preganglionic sympathetic block may have been complete enough to block any effective neurogenic vasoconstrictor response. Only in this patient was there marked increase in myocardial oxygen extraction, with transient ECG changes confirming the presence of myocardial hypoxia. This combination of high spinal anesthesia and mild blood loss could account for some of the more serious sudden hypotensive responses seen during surgery.

► [These observations emphasize the necessity for recognizing that although apparently only a portion of the body is anesthetized with spinal anesthesia, there is a serious compromise of the patient's ability to compensate. As indicated in this abstract, establishment and maintenance of a normovolemic state is essential. One must be careful, in addition, to avoid assuming that hypotension in a patient under spinal anesthesia is always a function of the anesthesia. Such an assumption encourages the indiscriminate and liberal use of vasopressor drugs and often endangers the patient suffering from hypovolemia, abnormal position or hypoventilation—Ed.]

## REGIONAL ANESTHESIA

**Death from Local Anesthesia** This report by the Anesthesia Study Committee of the New York State Society of Anesthesiologists<sup>6</sup> stresses need for safeguards in administration and supervision of local anesthesia. Five of six anesthetic deaths in one large hospital in one year were caused by local anesthesia.

Healthy woman, 34, received 100 mg pentobarbital sodium orally one hour before rhinoplasty and submucous resection, and 10 mg morphine sulfate and 0.4 mg atropine sulfate subcutaneously a half-hour later. After intranasal packing by the surgeon using 10% cocaine and 1:1000 epinephrine and submucous injection of 2% procaine hydrochloride and 1:50,000 epinephrine, the patient became apprehensive and restless. Meperidine hydrochloride, 100 mg, was injected subcutaneously to control marked excitement. The patient lay flat, she attempted to vomit at the beginning of operation. Immediately afterward she became completely still, radial pulse and heart sounds were absent and blood pressure was unobtainable. Resuscitation measures, including injections of epinephrine and nikethamide, artificial respiration ( \_\_\_\_\_ ) hic massage and direct injection c \_\_\_\_\_ the heart all failed. Autopsy failed.

Consistently safe local anesthesia depends on scrupulous-

(6) New York J Med 56:1504-1505, May 1, 1956

ly observing the following principles. Preanesthetic medication with a barbiturate is of no value in preventing shock-type reaction to local anesthetic drugs. Local anesthetics and epinephrine are highly potent drugs that should be as carefully measured and timed as spinal anesthetic agents. Cocaine is a potent vasoconstrictor if time is permitted for its full effect. Addition of epinephrine is unnecessary and synergizes the adrenergic effects of each drug. Demerol<sup>®</sup> is a poor choice for controlling excitement caused by emotion, cocaine, procaine or epinephrine. In absence of severe pain, a narcotic is never urgently required, particularly before determining the cause of the condition, of which excitement is only one sign, the subcutaneous route is too slow for prompt and effective control of excitement in the operating room.

Death from local anesthesia is preceded by warning signs unless a massive dose is inadvertently injected intravenously. Untoward effects precede cardiac arrest by several minutes, as in the case cited. If hypotension is detected early and corrected immediately, shock is readily aborted by ephedrine sulfate, 10-25 mg intravenously, when pulse rate is 60 or less, or by infusion of dilute neo-synephrine<sup>®</sup>, mephentermine or l-nor-epinephrine when pulse rate is over 60. The warning value of pallor and restlessness is generally ignored. A vasovagal episode of emotional origin can not always be differentiated from procaine shock, since both cause hypotension and bradycardia. Treatment must be instituted immediately even though doubt exists as to presence of procaine shock. Vasovagal faint can also be fatal, even with the patient in a horizontal position.

If cardiac arrest in this patient were the climax of ventricular fibrillation, based on adrenergic addition or synergism by epinephrine, cocaine, pain and fear, observation of blood pressure might have disclosed premonitory signs. The earliest sign of adrenergic reaction is hypertension, followed by hypotension. Either or both might be heralded or accompanied by cardiac arrhythmia. When stopping anesthetic administration or the operation does not halt an adrenergic reaction, intravenous injection of an adrenolytic agent, e.g., chlorpromazine or regitine<sup>®</sup> is indicated.

To make true the universal assumption that local anesthesia is the safest method requires more than preventing

injections that are inadvertently intravenous, too rapid or too great drug concentrations. Drug tolerance is unpredictable and reactions cannot be eliminated simply by rules, dosage or choice of other agents. The requisite usually disregarded is careful observation of pulse and blood pressure before and during induction and absorption of local anesthesia, especially when the patient is excited, restless, pale or vomiting. Otherwise, death from local anesthesia will occur, incorrectly labeled as unpredictable sudden and non-preventable 'idiosyncrasy,' 'hypersensitivity' or "cardiac arrest."

► [To those who assume that the use of local anesthetics eliminates the hazards of anesthesia the evidence presented here should be illuminating—Ed]

**Local Anesthesia in Newborn**, according to Richard E. Straith, Jack L. Teasley and Lawrence T. Moore\* (Detroit), is safer and less cumbersome than general anesthesia in correction of certain congenital deformities. It obviates need of parenteral fluid maintenance and allows use of epinephrine, which reduces blood loss in vascular tumors.

For best results in cleft lip and palate repair, operation should be done before age 3 months preferably at age 7-10 days provided weight is 6 lb and vital signs and fluid intake normal. Nembutal® or seconal® is given rectally 45 minutes preoperatively. Required depth of analgesia is achieved with demerol® given intramuscularly 15 minutes before surgery. For correction of cleft lips block anesthesia usually consists of 5 cc of 1% xylocaine® at each infraorbital foramen, in the base of the columella at each superior buccal fornix and at corners of the mouth, with a maximum of 10 cc. Adequate respirations with good color are found in almost all babies. Oxygen may be used nasally if necessary.

Gavage is begun almost immediately postoperatively. Recovery is usually uneventful. No death due to anesthesia occurred in more than several hundred cases of congenital deformity treated in this way.

► [The authors' experience with this type of anesthesia for newborns with congenital deformities is sufficient to encourage consideration of the method. However, certain assumptions made in support of the technique deserve comment. General anesthesia does not preclude the use of epinephrine or local anesthetic agents either to augment anesthesia or to diminish bleeding. Traditional practice often overlooks the possibility of

combination of local and general anesthesia. The authors discount the well established depressant effects of such narcotics as demerol® on respiration, cough reflex and circulation. Hypoventilation can exist in a significant degree without obvious decrease in rate of respiration or cyanosis. In an infant, decrease in respiratory rate and cyanosis would be late and ominous signs of trouble.—Ed.]

**New Method for Local Anesthesia in Peroral Endoscopy Preliminary Report.** For safer and more satisfactory anesthesia, Hubert J. Adler<sup>8</sup> (V A Hosp., Phoenix) uses a series of injections of procaine hyaluronidase mixture or xylocaine® to effect pharyngolaryngeal block, besides instilling cyclaine® pyribenzamine® into the tracheobronchial tree.

Injection is made in the superior laryngeal nerve at the hypothyroid ligament. The anterior, middle and posterior palatine nerves are blocked at the greater palatine canal, or the latter two nerves are blocked at the lesser palatine foramina and supplemented by infiltration around the incisive fossa. The glossopharyngeal nerve is blocked at the hilar area of the palatine tonsil, its terminals at the lingual tonsil. The superior laryngeal nerve again at the pharyngoepiglottic ligament, and, finally, the posterior wall of the hypopharynx is infiltrated.

The procedure takes about 12 minutes and gives anesthesia and relaxation of the epiglottis, larynx, hard and soft palates, uvula, anterior and posterior pillars, tonsils, base of tongue, hypopharynx, cricopharyngeal muscle and upper incisor teeth.

**Management of Pain in Peripheral Arterial Ischemia** is described by Philip M. Marcus<sup>9</sup> (Beverly Hills, Calif.). Continuous posterior tibial nerve block is performed by introducing behind the medial malleolus a plastic cannula with removable intravenous needle as stylet, and administering procaine through it as needed. Indications for the procedure are (1) severe pain in the distal foot with or without lesions and edema, (2) acute inflammation not yet localized and (3) sympathectomy ineffective or contraindicated because of uncontrolled diabetes or other disease. When pain is controlled with procaine, priscoline® is injected into the common femoral artery usually twice a day. Antibiotics and heparin can be given by the same route. Because of reflex arteriolar and capillary spasm with pain, sympathetic nerve block may be ineffective and by itself does not relieve pain.

<sup>8</sup> (8) J A M A 159 111 112 Sept. 10 1955  
(9) West J Surg 63 728 731 December 1955

During four to seven days of procaine management, acute inflammation subsides, systemic disease can be treated and subsequent sympathectomy or conservative amputation carried out more successfully. No amputation was required in 16 of 28 arteriosclerotics or in 11 of 23 diabetics treated

---

## HYPOTHERMIA

Feasibility of Partial Hepatic Resection under Hypothermia was tested in dogs by William F. Bernhard, James D. McMurrey and George W. Curtis<sup>1</sup> (Harvard Med. School). Histologic study of liver and postoperative liver function tests in dogs subjected to hypothermia with and without hepatic afferent occlusion disclosed no damage.

In normothermic animals with afferent hepatic vascular occlusion for one hour, mortality was 100%. Preoperative administration of antibiotics did not alter this result. Under hypothermia, vascular occlusion of the hepatic afferent artery for one hour was carried out successfully, with only 2 deaths in 27 dogs. There were no deaths in the last 20 consecutive dogs. No antibiotics were administered.

Liver resection seems feasible with a dry field, utilizing afferent vascular occlusion in hypothermia. Surgical indications for use of hypothermia might be extended to include patients with hepatocellular disease requiring anesthesia and surgery, patients with primary or secondary tumors of the liver, who might be treated successfully by liver resection, and patients with tumor extension to the portal vein who might not otherwise be considered capable of surviving operation.

Hypothermia seems superior to hypotensive technics as an adjunct to anesthetic management of patients. With hypotensive anesthesia, there is reduction in blood flow without simultaneous reduction in tissue metabolic requirements. This disadvantage, particularly in liver disease, does not occur with hypothermia, which also reduces systemic blood pressure. In extracardiac surgery, risk of cardiac arrhythmias is minimal, and thus should not negate use of hypothermia.

► [In the light of considerable evidence to the contrary the authors are optimistic about the minimal incidence of fibrillation associated with hypothermia in the absence of manipulation of the heart—Ed.]

(1) New England J. Med. 253:159-164 Aug. 4, 1955

**Role of Hypoxia in Hypothermic Cardiac Arrest in Heart Lung Preparation** Henry Badeer<sup>2</sup> (American Univ of Beirut), using a modified dog heart-lung preparation to allow direct measurement of coronary flow, induced hypothermia in dogs. Ventricular fibrillation occurred in 10 of 20 experiments. In control dogs the lungs were inflated with room air, and some air also bubbled through the venous return bottle. In a second series, oxygen inflation was used, the reservoir was saturated with oxygen and blood was pumped from the venous to the arterial side of the circuit to elevate aortic pressure and provide better coronary flow. The temperature causing cardiac arrest by fibrillation averaged 19.6 C under air inflation and 20.3 C with oxygen. Total coronary flow was 27% greater than before cooling in the control dogs and 36% greater in the oxygen series. Thus, when coronary flow during hypothermia is high, relative to demand, 100% oxygen does not affect the critical temperature that arrests the heart, hypoxia of the myocardium does not contribute to hypothermic cardiac arrest. Increased coronary flow during hypothermia seems due to decrease in resistance of coronary vessels. Thus there is increased flow despite the fall in mean arterial pressure, increased blood viscosity and reduced metabolic rate.

**Ventricular Fibrillation in Hypothermic State II Effect of Sinoauricular Node Blockade in Preventing Ventricular Fibrillation at Low Degrees of Body Temperature** A. Riberi, P. F. Grice and H. B. Shumacker, Jr.<sup>3</sup> (Indiana Univ.) previously demonstrated that procaine in the sinoauricular node is effective in preventing ventricular fibrillation caused by cardiac stimulation in dogs cooled to 24-28 C. Similarly in this series of 32 experiments, dogs were cooled to 19-22.5 C and a right cardiectomy performed after occlusion of both venae cavae. The myocardium stayed pink for a longer period following vena cava occlusion than at higher body temperatures. However, ventricular contractions were weaker and the rate slower than at higher temperatures, and several minutes occasionally elapsed before satisfactory contractions occurred following release of clamps, cardiac massage sometimes being necessary.

After procaine blockade of the sinoauricular node, the

<sup>2</sup>) Am J Physiol 183:119-120, October 1955.  
 Am Surgeon 21:1084-1090, November 1955.





**Role of Hypoxia in Hypothermic Cardiac Arrest in Heart-Lung Preparation.** Henry Badeer<sup>2</sup> (American Univ of Beirut), using a modified dog heart-lung preparation to allow direct measurement of coronary flow, induced hypothermia in dogs. Ventricular fibrillation occurred in 10 of 20 experiments. In control dogs the lungs were inflated with room air, and some air also bubbled through the venous return bottle. In a second series, oxygen inflation was used, the reservoir was saturated with oxygen and blood was pumped from the venous to the arterial side of the circuit to elevate aortic pressure and provide better coronary flow. The temperature causing cardiac arrest by fibrillation averaged 19.6 C under air inflation and 20.3 C with oxygen. Total coronary flow was 27% greater than before cooling in the control dogs and 36% greater in the oxygen series. Thus, when coronary flow during hypothermia is high, relative to demand, 100% oxygen does not affect the critical temperature that arrests the heart, hypoxia of the myocardium does not contribute to hypothermic cardiac arrest. Increased coronary flow during hypothermia seems due to decrease in resistance of coronary vessels. Thus there is increased flow despite the fall in mean arterial pressure, increased blood viscosity, and reduced metabolic rate.

**Ventricular Fibrillation in Hypothermic State II. Effect of Sinoauricular Node Blockade in Preventing Ventricular Fibrillation at Low Degrees of Body Temperature.** A. Riberi, P. F. Grice and H. B. Shumacker, Jr.<sup>3</sup> (Indiana Univ.) previously demonstrated that procaine in the sinoauricular node is effective in preventing ventricular fibrillation caused by cardiac stimulation in dogs cooled to 24-28 C. Similarly in this series of 32 experiments, dogs were cooled to 19-22.5 C, and a right cardiectomy performed after occlusion of both venae cavae. The myocardium stayed pink for a longer period following vena cava occlusion than at higher body temperatures. However, ventricular contractions were weaker and the rate slower than at higher temperatures, and several minutes occasionally elapsed before satisfactory contractions occurred following release of clamps, cardiac massage sometimes being necessary.

After procaine blockade of the sino-auricular node, the

(2) *Am J Physiol* 183: 119-120, October, 1955.  
(3) *Am Surgeon* 1: 1084-1090, November, 1955.

heart rate slowed precipitously with occasional cardiac standstill for three or four seconds P waves disappeared or were greatly reduced in voltage in almost all Except for those in which fibrillation took place, the hearts of the untreated animals seemed as regular in rhythm and as free from irritability as those treated with procaine Low voltage and inversion of ventricular complex occurring after cardiectomy usually disappeared with warming In both groups of animals, sudden cessation of respiration and cardiac standstill at times occurred during rewarming When cardiac standstill was imminent, it responded to epinephrine intravenously Nine of the 16 control animals had fibrillation, 1 had standstill and 6 survived the procedure and rewarming In the treated group, one animal had fibrillation during massage following release of occlusion One cardiac standstill occurred during rewarming

Fibrillation with right cardiectomy and prolonged inflow occlusion did not occur as frequently at these low temperatures as between 26-28°C Procaine injection of the sinoauricular node may prolong the safe period of vena cava occlusion and cardiectomy during hypothermia

#### Hematologic Changes in Hypothermic Dogs Tulio J

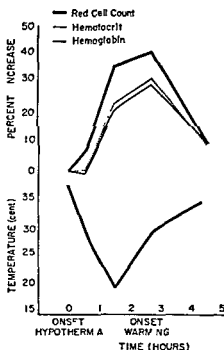


Fig 154—Changes in red blood cell count hematocrit and hemoglobin correlated with body temperature of dog showing rise in red cell values with cooling and return to normal with rewarming (Courtesy of Villalobos T J *et al* Proc Soc Exper Biol & Med. 89 192 196 June 1955)

## ANESTHESIA

Villalobos, Edward Adelson and Timothy G. Barila<sup>4</sup> (Walter Reed Army Hosp.) subjected nine dogs to hypothermia (62.6 F) under pentothal<sup>®</sup> anesthesia and drew periodic blood samples for counting and for clotting studies from a catheter in the femoral artery. Red blood cell count, hemoglobin concentration and hem-

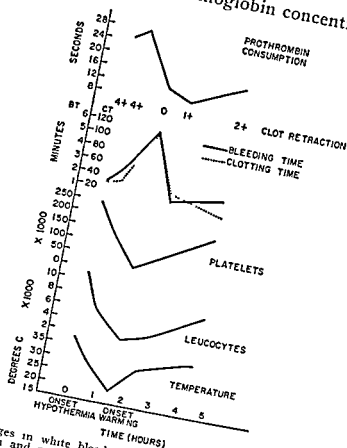


Fig 155—Changes in white blood cells, platelets, silicone clotting time, bleeding time, clot retraction and prothrombin consumption correlated with body temperature of dog. As platelets drop, all platelet functions are interfered with. Figure also shows hypercoagulability in 2 1/4 hour test of bleeding time and in 4 1/2 hour test of silicone clotting time. (Courtesy of Villalobos, T. J., et al. Proc Soc Exper Biol & Med 89:192-196, June 1955)

atocrit all rose, with maximal rise usually at or just before maximal fall in temperature (Fig 154). Hemoconcentration is probably due to temporary withdrawal of plasma, a concept supported by one experiment in which plasma and red blood cell volume were measured. White cells of all types nearly disappeared, the values returning to normal within one-half hour of rewarming. Absence of a shift to the left suggests that the reappearing cells were not new ones. Necrotic red cells appeared at the time of maximal cooling.

(4) Proc Soc Exper Biol & Med 89:192-196, June, 1955

and became more numerous during warming. Platelets almost disappeared, and the degree of thrombocytopenia seemed adequate to account for concurrent prolongation of clotting time, decrease in prothrombin consumption, loss of clot retraction and increase in bleeding time (Fig 155). Warming resulted in rise in platelet count and in some, hypercoagulability not explained by platelet count or plasma prothrombin activity. Hypothermia caused no significant change in plasma prothrombin activity, fibrinogen levels or fibrinolytic activity.

**Hypothermia in Surgery** Analysis of 100 Cases is presented by Henry Swan, Robert W. Virtue, S. Gilbert Blount, Jr., and Lorence T. Kircher, Jr.<sup>5</sup> (Univ. of Colorado). Indications for hypothermia are (1) open heart procedures that can be approached from the right side and performed in no more than eight minutes, (2) cyanotic heart disease and severe tachycardia with consequent improvement of operative risk and (3) such prolonged procedures as portocaval shunt for cirrhosis, in which cold might be less toxic to the liver than any pharmacologic agent. Acute hypothermia above 26°C itself carries a low risk.

Scopolamine is used with barbiturates or opiates for premedication. Ether is the agent of choice. Needle electrodes placed in the skin are better than ordinary ECG lead supports, which may constrict the limbs and lead to peripheral neuropathies. When anesthetized, the patient is placed in a cold water tub. Curare is given, and, when the temperature begins to drop, ice is added. At about 31°C, ether is stopped and hyperventilation carried out until circulatory occlusion is over. After the patient is placed on the operating table, the temperature tends to drop two thirds of the amount that it dropped while he was in the tub. Due to diminution of circulating plasma volume during hypothermia, more than the calculated blood loss may have to be replaced.

Half the patients show auricular fibrillation at below 29°C. About five minutes before circulatory occlusion, more curare is given to prevent diaphragmatic contraction when blood flow resumes. With pH at least 7.5 at time of occlusion, incidence of fibrillation is reduced. During occlusion 100% oxygen alone is given, supplemented if necessary by nitrous oxide. Warming is started at closure of the cardiectomy.

Villalobos, Edward Adelson and Timothy G. Barila<sup>4</sup> (Walter Reed Army Hosp.) subjected nine dogs to hypothermia (62.6 F.) under pentothal<sup>2</sup> anesthesia and drew periodic blood samples for counting and for clotting studies from a catheter in the femoral artery.

Red blood cell count, hemoglobin concentration and hem-

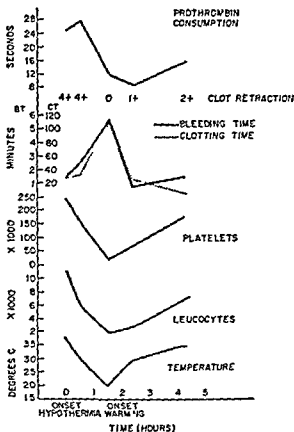


Fig. 155 —Changes in white blood cells, platelets, silicone clotting time, bleeding time, clot retraction and prothrombin consumption correlated with body temperature of dog. As platelets drop, all platelet functions are interfered with. Figure also shows hypercoagulability in 2½ hour test of bleeding time and in 4½ hour test of silicone clotting time. (Courtesy of Villalobos, T. J., et al. Proc. Soc. Exper. Biol. & Med. 89:192-196, June, 1955.)

atocrit all rose, with maximal rise usually at or just before maximal fall in temperature (Fig. 154). Hemoconcentration is probably due to temporary withdrawal of plasma, a concept supported by one experiment in which plasma and red blood cell volume were measured. White cells of all types nearly disappeared, the values returning to normal within one-half hour of rewarming. Absence of a shift to the left suggests that the reappearing cells were not new ones. Nucleated red cells appeared at the time of maximal cooling

(4) Proc. Soc. Exper. Biol. & Med. 89:192-196, June, 1955

and became more numerous during warming. Platelets almost disappeared, and the degree of thrombocytopenia seemed adequate to account for concurrent prolongation of clotting time, decrease in prothrombin consumption, loss of clot retraction and increase in bleeding time (Fig 155). Warming resulted in rise in platelet count and in some, hypercoagulability not explained by platelet count or plasma prothrombin activity. Hypothermia caused no significant change in plasma prothrombin activity, fibrinogen levels or fibrinolytic activity.

**Hypothermia in Surgery.** Analysis of 100 Cases is presented by Henry Swan, Robert W. Virtue, S. Gilbert Blount, Jr., and Lorence T. Kircher, Jr.<sup>5</sup> (Univ. of Colorado). Indications for hypothermia are (1) open heart procedures that can be approached from the right side and performed in no more than eight minutes, (2) cyanotic heart disease and severe tachycardia with consequent improvement of operative risk and (3) such prolonged procedures as portocaval shunt for cirrhosis, in which cold might be less toxic to the liver than any pharmacologic agent. Acute hypothermia above 26 C itself carries a low risk.

Scopolamine is used with barbiturates or opiates for premedication. Ether is the agent of choice. Needle electrodes placed in the skin are better than ordinary ECG lead supports, which may constrict the limbs and lead to peripheral neuropathies. When anesthetized, the patient is placed in a cold water tub. Curare is given, and, when the temperature begins to drop, ice is added. At about 31 C, ether is stopped and hyperventilation carried out until circulatory occlusion is over. After the patient is placed on the operating table, the temperature tends to drop two thirds of the amount that it dropped while he was in the tub. Due to diminution of circulating plasma volume during hypothermia, more than the calculated blood loss may have to be replaced.

Half the patients show auricular fibrillation at below 29 C. About five minutes before circulatory occlusion, more curare is given to prevent diaphragmatic contraction when blood flow resumes. With pH at least 7.5 at time of occlusion, incidence of fibrillation is reduced. During occlusion 100% oxygen alone is given, supplemented if necessary by nitrous oxide. Warming is started at closure of the cardiectomy.

(5) Ann Surg 142:382-400 September 1955

Blood pressure should be audible before the chest is closed, to reveal latent bleeding. Usual wakening temperature is 34 C. Difficulty of assessing adequacy of blood replacement and danger of shock during the warming period have led to use of pre- and postoperative blood volume measurements.

To minimize the danger of coronary air embolism, the cardiotomy is positioned at the uppermost portion of the heart. A clamp is placed to occlude the coronary ostia, the heart cavity is filled with Ringer's solution and manual compression of the heart and expression of visible bubbles in the coronaries are performed before cardiotomy is closed and circulation re-established.

Manual cardiac compression successfully revived all seven patients with ventricular standstill. Ventricular fibrillation was usually successfully treated by electric defibrillation after initiation of manual compression. If this failed, KCl was also used. If the heart became flabby with fine fibrillations, epinephrine was injected. Warming was started immediately. A diathermy coil wrapped around the pelvis proved more effective than a warming mattress alone. Quinidine was not used prophylactically. Neostigmine injected into the root of the clamped aorta after inflow occlusion probably reduced incidence of fibrillation.

Nonfatal complications included superficial burns from diathermy or mattress, thrombophlebitis, wound infection, pulmonary complications (the largest single group of complications), neurologic sequelae of peripheral type and anuria (one case). There were no instances of delayed wound healing.

Of 44 patients with single cardiac defects, 7 died, of 15 with multiple defects, 5 died, and of 21 with closed cardiac procedures, 7 died. In the noncardiac group, 3 of 20 died. Of the 22 deaths 8 were unrelated to hypothermia. Five patients died of unconverted ventricular fibrillation, in five fibrillation was converted, but they died of failure or hemorrhage. In one, cardiac standstill was converted but was later followed by failure. In two patients with thromboembolism and one with heart failure, death was possibly related to hypothermia. Disturbance of myocardial function is almost the only cause of death in patients having cardiac surgery during hypothermia. Temperatures lower than 26 C and occlusion times longer than eight minutes sharply

increase the risk. Of the 15 instances of fibrillation, 5 occurred during thoracotomy, 3 during cardiac surgery and 7 immediately after release of circulatory occlusion. Four patients died of postoperative hemorrhage. A posthypothermic hemorrhagic state has not been documented. Of 30 patients not receiving neostigmine, 9 had fibrillation; of 29 who received the drug, 3 fibrillated though some of the fibrillations occurred before circulatory occlusion, at which time the drug was given. Of 20 patients with noncardiac procedures, none died of causes related to hypothermia, and none fibrillated.

Hypothermia is effective and safe in congenital lesions that can be repaired through a right heart approach and is the method of choice in isolated valvular or infundibular pulmonary stenosis and in interatrial septal defect.

---

## CIRCULATION

Circulatory Disturbances during Cerebral Angiography were studied by Allan S. Brown<sup>6</sup> (Royal Infirmary, Edinburgh) in 100 patients. Anesthesia was induced by thiopentone and d-tubocurarine, with maintenance by nitrous oxide-oxygen supplemented by trichlorethylene. After local infiltration into the tissues around the carotid or vertebral artery at the intended site of puncture, 8-10 ml. of 35% uriodone was injected into the lumen of the artery. Immediately after injection, there was a transient rise in blood pressure and then a transient fall of 5-10 mm., in contrast with the immediate rise in blood pressure in unanesthetized subjects. With forceful injection of the dye into the vertebral artery, transient fall of blood pressure and slowing of pulse and respiratory rate occur only when retrograde filling of the contralateral vertebral artery takes place, coinciding with the time taken for the solution to reach the medulla, which may become anoxic.

Immediate fall in blood pressure of 20-100 mm. Hg, lasting from 5-15 minutes, with moderate hypotension, to several hours, with severe hypotension, was noted in 25 patients with recent spontaneous subarachnoid hemc...

(6) *Anaesthesia* 10:346-358, October, 1955.



## ANESTHESIA

demonstrated in 20 as due to aneurysm. This circulatory reaction was not seen in six other patients with aneurysms nor in five with arteriovenous malformation.

The reaction seems to be associated with vascular disturbance of the preoptic area of the hypothalamus, increasing the anoxia to a level where spontaneous vasomotor control is lost. It is most striking in aneurysm of the anterior communicating artery, with disturbed blood supply to the anterior portion of basal ganglions and hypothalamus. Vessels in the region of the ruptured aneurysm probably go into prolonged spasm after stimulation such as caused by the irritant dye.

A second pattern of circulatory disturbance consisted of gradual fall of blood pressure, starting 5 minutes after induction and continuing for 5-10 minutes, and again the more profound fall lasted longer. This response was noted in 43 patients with spontaneous subarachnoid bleeding and in 7 of 57 patients with other lesions, and was probably due to increased vascular permeability and progressive cerebral edema. Consciousness may be depressed beyond time of return to normal tension, contrary to the immediate type reaction.

Neither of these circulatory derangements is accompanied by significant change in pulse or respiratory rate unless the fall in blood pressure is severe. There is no peripheral vasoconstriction. If surgical technic is truly atraumatic, early treatment of hypotension, whatever its etiology, makes the dangers of cerebral angiography negligible. No serious transient or permanent complications occurred in over 350 patients.

**Hemodynamic Effects of Ether Anesthesia and Surgery**  
in 11 Cases were studied by Grant Fletcher, John W. Penland and Earl W. Wood<sup>7</sup> (Mayo Clinic and Found). The findings suggest that ether is not a direct myocardial stimulant in adults and that early increases in cardiac output noted in a few patients are related to episodes of marked excitement during induction. Decreases in cardiac output occurred uniformly in patients with relatively large and sustained increases in central venous pressure, compatible with the suggestion that ether is a direct myocardial depressant.

(7) *Anesth & Analg* 35 18 32, Jan Feb, 1956

However, dynamic relations of cardiac output, pulse rate and stroke volume were not significantly altered from those found in normal unanesthetized man. There was no evidence that light ether anesthesia caused significant decreases in cardiac reserve.

The nearly uniform decreases in systolic and mean blood pressure in the radial artery during the second and third hours of anesthesia were related to changes in cardiac output and peripheral resistance. No evidence was found that the fall in systolic blood pressure is due to decrease in peripheral resistance as a result of systemic vasodilatation.

Correlation between cardiac output and calculated central blood volume before and during anesthesia was similar to that in unanesthetized man. No particular significance is attached to the increase in mean central blood volume index during the first hour of anesthesia.

The data demonstrate that the clinical signs usually available, viz., pulse rate, blood pressure and respiration, indicate remarkably well the over all hemodynamic picture in patients receiving light ether anesthesia.

**Relation between Hemodynamic and Plasma Volume Alterations during General Anesthesia in Man.** During surgical operations and ether anesthesia, reduction in blood volume is too great to be explained by external blood loss and probably results from loss of plasma water to extracellular fluid. The most likely cause is a disparity between capillary filtrations and reabsorption and lymphatic return, caused in turn by changes in blood pressure. Hence, hemodynamic alterations produced by general anesthesia may be of prime importance in determining net loss or gain of plasma water from capillary blood. Henry L. Price, Martin Helrich and Eugene H. Conner<sup>8</sup> (Univ. of Pennsylvania) studied changes in blood and plasma volume observed during cyclopropane ether and thiopental anesthesia in 31 healthy patients scheduled for elective operations.

Atropine or scopolamine had no measurable effect on plasma volume or arterial pressure. Addition of morphine was associated with significant increase in plasma volume. No consistent change in arterial pressure occurred after morphine, though usually there was a decrease. In patients lightly anesthetized with cyclopropane, change in plasma

(8) J. Clin. Invest. 35:125-131, January, 1956.

## ANESTHESIA

volume was insignificant and arterial pressure was not consistently altered. Venous pressure, however, increased in all cases (average, 7.9 cm. H<sub>2</sub>O). Those deeply anesthetized with cyclopropane (requiring manually controlled positive pressure respiration) exhibited a significantly reduced plasma volume with consistently increased arterial and venous pressures (+20 mm. Hg and +14.2 cm. H<sub>2</sub>O, respectively).

In the "early" period (17-35 minutes after induction, during which most patients exhibited excitement or other undesirable effects) of diethyl ether anesthesia, there was a significant decrease in plasma volume, with consistently increased arterial and venous pressures. The Pco<sub>2</sub> averaged 56 mm. Hg and oxygen saturation 87%. After establishment of anesthesia, all values began to revert toward normal. Plasma volume increased, although it remained significantly reduced as late as 80 minutes after induction. Changes in arterial pressure were completely reversed and in venous pressure, partially so, in the "late" period. Oxygen saturation averaged 97% at this time and Pco<sub>2</sub>, 57 mm. Hg.

With thiopental-nitrous oxide, significant increase in plasma volume occurred, with a consistent decrease in arterial pressure, but no consistent change in venous pressure. Most of the change in plasma volume occurred within the first half hour. Arterial Pco<sub>2</sub> averaged 46 mm. Hg and oxygen saturation, 99%.

Operation had no consistent effect on plasma volume or arterial or venous pressures. In some instances, decrease in plasma volume coincided with the beginning of operation; this was always accompanied by increase in arterial pressure and usually in venous pressure. On recovery from anesthesia, values tended to return to pre-anesthesia levels, but plasma volume was usually less.

The clinical significance of these observations is difficult to determine, it may be supposed that thiopental anesthesia and morphine result in partial depletion of extravascular extracellular fluid volume, whereas cyclopropane and ether do not. Cyclopropane or ether might therefore be better tolerated than thiopental by patients with depleted extracellular fluid volume. In support of this view, it has been found that pentobarbital, whose hemodynamic effects re-

semble those of thiopental, reduces rate of restoration of plasma volume after hemorrhage in dogs, cats and rabbits

**Blood Volume Studies Utilizing Radiochromium 51 Method and Its Application to Anesthesiology** Multiplicity of suggested methods and subsequent controversy about them have cast doubt on accuracy and utility of technics for measuring blood and plasma volume, especially with substances with affinity for plasma proteins John Abajian, Jr, Edward Brazell, Ernest L Mills and O S Peterson, Jr<sup>9</sup> (Univ of Vermont) determined blood volume by tagging red blood cells, which respect their boundary membranes better than plasma proteins, which usually show definite disappearance curves at a constant blood volume Radiochromium 51 firmly unites with red blood cells with little leakage in vivo A modification of the Read method was used

**TECHNIC**—To a plastic bag or 50 cc syringe is added 2 cc sodium chromate 51 solution containing about 100  $\mu$ c and 0.5 cc heparin solution, 40–50 cc blood is withdrawn into the bag (or syringe), and this is thoroughly mixed and incubated at 37 C for 30 minutes The uptake of chromium by the red blood cells is then fixed by addition of ascorbic acid After a background sample is withdrawn about half this blood is injected and a sample withdrawn after 15 minutes All samples are centrifuged 30 minutes, the hematocrit read the plasma expressed and the red blood cell mass counted for radio activity in a scintillation detector The red blood cell volume is determined by dividing the formula for the total counts injected by the counts minus background per volume in the sample of the patient Repeated determinations and addition of known quantities of blood to the circulation yielded an error of 4–6% in the method

Accuracy and ease of determining pre and postoperative blood volumes make this method useful to the anesthesiologist

**Blood Volume Determinations in Operative Period** Convenient, Simplified Procedure, using radioactive iodinated serum albumin is described by Carl E Wasmuth Otto Glasser, Walter E H Laude and Ranson L Smith<sup>1</sup> When the accuracy of the method was tested against the Evans blue method, the mean difference in estimates was 3.7% Determinations done after measured blood donations showed a mean difference between observed and estimated losses of 7.8% Calibrated syringes containing the isotope are kept

(9) Anesthesiology 16:733–737, September, 1955

(1) Cleveland Clin Quart 22:124–130, July, 1955

in the refrigerator at all times, and determinations can be done efficiently and repeated, without interference with the use of other colorimetric laboratory procedures

Preoperative blood volume determinations are of value particularly in the chronically ill and aged for the recognition and treatment of contracted blood volumes, which make patients prone to circulatory collapse during induction and deepening of anesthesia. Also, by repeated comparative de-

HEMOGLOBIN AND HEMATOCRIT VALUES COMPARED WITH BLOOD VOLUME IN VARIOUS CONDITIONS AND STAGES OF SURGICAL PROCEDURE

Case No	Status		Age (yr)	Hemoglobin Gm/100 ml	Hematocrit %	Blood Volume ml/Kg
1	Preoperative	Bleeding gastric ulcer	41	13.5	47	47
2	Preoperative	Carcinoma of colon	82	13.2	44	58
3	Preoperative	Embolus femoral artery	—	14.2	54	80.5
	Postoperative	Arterial embolotomy	—	13.5	49	74
4	Preoperative	Diabetes and gangrenous leg	—	15	48	47
5	Postoperative	Retropertoneal leiomyosarcoma	—	9.5	27	80.5

terminations in the postoperative period, blood lost during surgery can be accurately and repeatedly measured and replacement made according to the amount needed

**Beneficial Action of Pretreatment with Chlorpromazine on Survival Following Graded Hemorrhage in the Rat** was investigated by S. G. Hershey, I. Guccione and B. W. Zweifach<sup>2</sup> (New York Univ.). They subjected rats to five grades of hemorrhagic hypotension, treating one group with chlorpromazine, which can eliminate or attenuate many vascular phenomena associated with the irreversible phase of shock. Chlorpromazine (2.5 mg/100 Gm body weight) was given intramuscularly 30 minutes before anesthesia with pentobarbital sodium. Bleeding was done through a cannulated

carotid artery into a take-up reservoir filled with heparin in saline. At end of the hypotensive period, each animal received graded infusion of the remainder of the blood in the reservoir. Rats alive 24 hours after the end of the experiment were designated survivors. The volume of blood spontaneously taken from the reservoir served as an index of the degree of vascular decompensation.

Survival percentages for chlorpromazine-treated rats were consistently higher than controls in all except the group with severest hemorrhage. In the control series, maximum blood output volume was greater and less blood was subsequently taken up by survivors, compared to rats that died. These phenomena were present, although less strikingly so, in the treated series. Treated survivors required little or no blood from the reservoir to sustain blood pressure at selected levels. As indicated by the blood take-up data, chlorpromazine seems to blunt the progressive decompensatory vascular tendency of lethal shock, one feature of which is splanchnic pooling of blood. Protected animals showed no peripheral cyanosis, but sustained the emptying and refill capacity of superficial vessels. Central nervous system response to stress, as indicated by more regular and less rapid respirations than in controls, seemed beneficially modified by chlorpromazine. Autopsies revealed hemorrhagic congestion of liver, spleen, small intestine and, to lesser extent, of lungs and hemorrhage into the intestine in control rats that died, less abnormal change in control survivors and no gross pathologic conditions in protected survivors.

**Hemodynamic and Metabolic Interrelationships in Activity of Epinephrine, Nor-Epinephrine and Thyroid Hormones** were studied in experiments on 31 thyroid-fed and 27 euthyroid dogs by William R. Brewster, Jr., James P. Isaacs, Patricia F. Osgood and Thelma L. King<sup>3</sup> (Harvard Med School). Serum protein bound iodine concentrations of euthyroid dogs averaged  $17 \mu\text{g}/100 \text{ ml}$ . After thyroid feeding, average serum protein bound iodine concentrations were, at 7-10 days, 166, 11-15 days 181 and 18-22 days,  $169 \mu\text{g}/100 \text{ ml}$ . Thyroid feeding caused the classic hemodynamic and calorigenic effects of hyperthyroidism, including highly significant increases in heart rate, oxygen

(3) *Circulation* 13:120 January, 1956

consumption, cardiac index and effective ventricular stroke

To differentiate between effects of l-epinephrine and l-nor-epinephrine and those of thyroid hormones, reflex release of epinephrine was abolished in euthyroid and thyroid-fed dogs by total epidural preganglionic sympathetic block, by injection of 0.45% procaine hydrochloride solution. This abolished metabolic and hemodynamic effects of thyrotoxicosis. During total sympathetic block, no significant difference was noted in oxygen consumption, cardiac indexes, heart rates, average right or left atrial mean pressures, ventricular stroke and arteriovenous oxygen differences in thyroid-fed dogs and those of euthyroid animals.

All parameters of activity of l-epinephrine and l-nor-epinephrine were increased by higher concentrations of thyroid hormones. Infusion of l-epinephrine or l-nor-epinephrine into thyroid-fed dogs with total sympathetic block resulted in a rise in oxygen consumption, heart rate, cardiac index and ventricular stroke per unit of filling pressure, significantly greater than that seen during infusion in a comparable series of euthyroid dogs. Whereas infusion of l-epinephrine or l-nor-epinephrine in euthyroid or thyroid-fed animals resulted in equivalent inotropic, chronotropic or calorogenic effects, there was a fundamental difference in glycogenolytic effects, as reflected in blood and serum concentrations of lactate, pyruvate and sugar. Infusion of l-epinephrine consistently resulted in a rise in serum lactate, pyruvate and blood sugar levels, whereas l-nor-epinephrine, despite its equal calorogenic effect, caused a fall in blood and serum concentrations of these substances. Normal values of serum lactate, pyruvate and blood sugar in thyroid-fed animals in the control state suggest that l-nor-epinephrine is the predominant mediator of physiologic effects of thyrotoxicosis related to activity of the sympathetic nervous system.

The authors conclude that there is a dynamic interrelation between thyroid hormones and l-epinephrine and l-nor-epinephrine. Physiologic effects of thyrotoxicosis do not result from isolated action of thyroid hormones per se, but are due to physiologic effects of l-epinephrine and l-nor-epinephrine as augmented by thyroid hormones. Optimal concentrations of adrenocortical steroids are essential for

dynamic activity of the hormones of the thyroid and sympathetic nervous system to become manifest.

**Effects of Anesthetic Agents and Relaxants on Vascular Tone Studies in Sandison-Clark Chambers.** Investigations on rabbits with the pre-formed ear chamber are reported by H. A. S. van den Brenk, N. M. Cass and R. D. Chambers.<sup>4</sup> Ear chambers are ideal for direct visual observation of effects of drugs on arteries and arterioles. Observed changes in caliber of capillaries and noncontractile vessels, however, do not present a true picture of dynamic changes in tissues that can increase or decrease in total volume. Any interpretation of changes in contractile vessels must consider variations in normal tone, particularly those brought about by phasic physiologic variation, i.e., "vasomotion." During anesthesia, hypoxia and hypercapnia, inadvertently produced, cause marked variation in vascular tone, as do changes in systemic arterial pressure.

For the inhalation anesthetic agents tested, except nitrous oxide, a light plane of anesthesia invariably caused arterial constriction, supporting the current view that anesthetics initially stimulate the vasomotor center. Arterial dilatation followed deep anesthesia with ether and chloroform. These changes are reversible by altering the plane of anesthesia. With nitrous oxide anesthesia, all changes in vascular caliber observed can be explained by changes in oxygenation and carbon dioxide retention.

Arterial constriction caused by cyclopropane agrees with the present clinical impressions that cyclopropane anesthesia, without CO<sub>2</sub> retention, is not accompanied by increased arteriolar bleeding. Return of consciousness and voluntary movements following anesthesia were invariably accompanied by marked increase in vascular tone—always in excess of the initial tone before anesthesia.

Thiopentone caused diminished vascular tone and  $\beta$ ,  $\beta$ -ethylmethyl glutarimide (megimide), a barbiturate antagonist, caused arterial constriction, reversed by additional doses of thiopentone.

Investigation of effect of relaxant drugs on vascular tone in the conscious animal is difficult because artificial respiration is required, which produces a complicating effect by

(4) Brit. J. Anaesth. 28:98-112, 1956.



causing nervous stress, with intermittent positive pressure respiration, as used, venous return is said to be impaired. Results suggest that d-tubocurarine, which causes diminution in vascular tone, depresses preganglionic sympathetic synapses without preliminary stimulation. This depression is not complete with a dose that causes respiratory paralysis, since subsequent painful stimulus caused intense constriction.

Gallamine triethiodide seemed to cause preliminary stimulation before depression. Again, block was incomplete, as pain caused constriction, but not comparable to that produced by a similar pain stimulus after paralysis had worn off. Suxamethonium caused profound constriction in a conscious animal under artificial respiration. When the drug was preceded by a hypnotic dose of thiopentone, and after respiration was artificially stabilized, the constriction was still present. This constriction is not an artifact due to respiratory embarrassment or nervous excitation, which suggests either a direct effect on vascular smooth muscle or sympathetic ganglionic stimulation. The central effect was abolished by blocking vasomotor nerves at the base of the ear, with consequent reduction in tone. Suxamethonium still caused profound vascular constriction followed by gradual return to the initial dilated state, suggesting direct stimulation of vascular smooth muscle.

Arterial dilation followed the exhibition of hexamethonium in accordance with its ganglion blocking properties. A subsequent painful stimulus caused minimal change in caliber, indicating a block more complete than that apparently produced by curare and gallamine.

Use of External Electric Pacemaker in Cardiac Arrest of various types is described by Paul M. Zoll, Arthur J. Linenthal, Leona R. Norman, Milton H. Paul and William Gibson<sup>5</sup> (Harvard Med. School). The instrument was used to resuscitate 27 patients from Stokes-Adams attacks due to ventricular standstill in 24 Stokes-Adams attacks due to ventricular tachycardia or fibrillation in 14 patients were not stopped. In five patients with frequent attacks due to multifocal ventricular tachycardia or fibrillation continued external stimulation prevented recurrence. Stimulation was continued after resuscitation in 22 patients for as long as

109 hours. Of 27 patients resuscitated, 10 (4 still alive) survived 1-29 months. Eight lived 1½-16 days, five lived 1-11 hours, and four did not survive the initial stimulation. Of 23 dead, 8 died from Stokes-Adams attacks because the pacemaker was not applied during the fatal attack, because the fatal attack was due to ventricular tachycardia or fibrillation or because of irreversible cerebral damage before electric stimulation was applied.

External electric stimulation was effective repeatedly (more than 100 times) in resuscitating three patients with ventricular standstill due to reflex vagal stimulation. Two patients with attacks of syncope due to digitalis and two with ventricular standstill after procainamide intravenously were resuscitated immediately several times.

In two patients with unexpected ventricular standstill during cardiac surgery, effective ventricular beats were produced by external and direct stimulation, but both died because of unsuccessful surgery. Complete recovery followed external resuscitation in three patients reported by others. Resuscitation was unsuccessful in eight patients (after delays of a few minutes to two hours) with unexpected circulatory arrest during surgical procedures.

Treatment for standstill—the most common cause of circulatory arrest—should be started immediately unless the mechanism is known to be fibrillation. While awaiting the electric pacemaker, which can be applied in 30-40 seconds, the heart should be stimulated by slapping the precordium forcefully, by cardiac needle puncture or by cardiac massage through the diaphragm, when the abdomen is open. Auxiliary measures such as artificial respiration with oxygen, blood transfusion and vasodepressor drugs may be necessary. If the initial mechanism is ventricular fibrillation or if the pacemaker fails to resuscitate within one minute from onset of arrest, the chest must be opened promptly for heart massage. If fibrillation persists, potassium chloride, procaine or procainamide can be injected into the heart, or countershock (60 cycles a c, 120-150 volts, 0.1 second) can be applied across large electrodes.

Ventricular standstill may persist despite effective massage, may recur after massage or may follow defibrillation. The electric pacemaker can then be applied directly to the heart and epinephrine hydrochloride (0.1-0.5 ml of 1:1000).

aqueous solution) injected into the left atrial or left ventricular cavity. If resuscitation is successful, the patient must be under constant observation for two or three days, because arrest may recur. A monitor of cardiac activity should be used to signal cessation of circulation immediately, and the electric pacemaker should be attached and ready for instant use.

► [There is universal agreement that delay in restoring effective heart action cannot be tolerated. Since the pacemaker is ineffective in treatment of fibrillation, and as fibrillation cannot be detected in the absence of an electrocardiogram or an open chest, one finds it difficult to condone any delay in opening the chest in circumstances of cardiac arrest to try pounding the chest wall, stimulation by the pacemaker and so on—Ed.]

**Cardiac Arrest. Further Studies on Effect of pH Changes on Vagal Inhibition of the Heart** are reported by Gilbert S. Campbell<sup>6</sup> (Univ. of Minnesota). In dogs, hypercapnia alone or hypercapnia plus hypoxia augmented cardiac inhibition during faradic vagal stimulation. Hypoxia did not increase the effect of vagal stimulation, in fact, hypoxia may have lessened it. With this background, studies were made in which blood pH was depressed by administration of carbon dioxide, hydrochloric acid or lactic acid, and others in which it was elevated by mechanical hyperventilation or sodium bicarbonate. Variables (blood  $P_{CO_2}$ , bicarbonate level or blood pH), altered by increased  $CO_2$  responsible for increased cardiac inhibition caused by faradic vagal stimulation or acetylcholine injection, were determined. In general, alteration in cardioinhibitory effects of either faradic vagal stimulation or acetylcholine can be correlated with changes in blood pH.

The well documented observation that optimal cholinesterase activity is between pH 7.5 and 8.5 was used in interpretation of results. In the presence of elevated blood pH, cholinesterase should be more effective in inhibiting acetylcholine (either endogenous, released by vagal stimulation, or exogenous, from injected acetylcholine) than it would be at normal blood pH. With an elevated blood pH, therefore, cardioinhibitory effects of vagal stimulation or acetylcholine should be decreased. Conversely, as blood pH is decreased with carbon dioxide, hydrochloric acid or lactic acid, acetylcholine is less rapidly hydrolyzed by cholinesterase than it was at normal blood pH. Subsequently, cardioinhibi-

tory effects are enhanced in the presence of an acid blood pH. During vagal stimulation, the endogenous release and cardioinhibitory effect of acetylcholine are dependent on blood pH and particularly the cellular pH of the effector organ, in this case the heart. The pH measurements were made on arterial blood, and critical values for intracellular hydrogen ion concentration in the heart are not known. A qualitative relation may be assumed, but evidence for quantitative differences are real.

Laboratory evidence for potentiation of cardioinhibitory effects during chemical and faradic vagal stimulation have a bearing in surgery. Because vagal stimulation is inadvertently caused by endotracheal intubation or extubation, when the patient is rather light and reflexes less depressed, occasional cardiac arrests at such times are probably more than coincidental. Operative manipulation in the thorax or abdomen also causes varying degrees of vagal stimulation, especially along the afferent pathways. Under conditions of an acid blood pH, potentiation of such reflexes may prove fatal. Possibly avoidance of acidosis during operative procedures will decrease incidence of cardiac arrest. Many surgeons and anesthesiologists have noted improved cardiac tone and increased cardiac rate associated with active "bagging" of patients undergoing intrapleural surgery, especially when the lungs had previously been inadequately ventilated. The improved cardiac status is probably partly due to correction of hypercapnia and not solely to correction of hypoxia.

**Cardiac Arrest.** A. O. Singleton, Jr., and A. W. DeLoach<sup>7</sup> (Univ. of Texas) stress that the main problem lies in prevention and recognition rather than active treatment, even though this may save some lives. The usual cause of cardiac arrest is anoxia or hypoxia, the latter may be caused or accentuated by anemia, shock or incomplete blood replacement. Overdoses of anesthetics and multiple agents have often been incriminated, but cardiac arrest has occurred with every type of anesthetic, including local and spinal. Cyclopropane, ethyl chloride and chloroform are believed to sensitize the heart directly to epinephrine and thus bring about cardiac arrest. Hypersensitivity to anesthetics is a possible factor in a few cases.

(7) Texas Rep. Biol. & Med. 13:1027-1034, Winter, 1955.

aqueous solution) injected into the left atrial or left ventricular cavity. If resuscitation is successful, the patient must be under constant observation for two or three days, because arrest may recur. A monitor of cardiac activity should be used to signal cessation of circulation immediately, and the electric pacemaker should be attached and ready for instant use.

► [There is universal agreement that delay in restoring effective heart action cannot be tolerated. Since the pacemaker is ineffective in treatment of fibrillation, and as fibrillation cannot be detected in the absence of an ECG record or an open chest, one finds it difficult to condone opening the chest in circumstances of cardiac arrest to try chest 'all,' stimulation by the pacemaker and so on.—Ed.]

**Cardiac Arrest: Further Studies on Effect of pH Changes on Vagal Inhibition of the Heart** are reported by Gilbert S. (University of Minnesota). In dogs, hypercapnia plus hypoxia augmented cardiac inhibition by faradic vagal stimulation. Hypoxia did not modify the effect of vagal stimulation; in fact, hypoxia may have elevated it. With this background, studies were made in which blood pH was depressed by administration of carbon dioxide, hydrochloric acid or lactic acid, and others in which it was elevated by mechanical hyperventilation or sodium bicarbonate. Variables (blood  $\text{PCO}_2$ , bicarbonate level or blood pH), altered by increased  $\text{CO}_2$  responsible for increased cardiac inhibition caused by faradic vagal stimulation or acetylcholine injection, were determined. In general, alteration in cardioinhibitory effects of either faradic vagal stimulation or acetylcholine can be correlated with changes in blood pH.

The well documented observation that optimal cholinesterase activity is between pH 7.5 and 8.5 was used in interpretation of results. In the presence of elevated blood pH, cholinesterase should be more effective in inhibiting acetylcholine (either endogenous, released by vagal stimulation, or exogenous, from injected acetylcholine) than it would be at normal blood pH. With an elevated blood pH, therefore, cardioinhibitory effects of vagal stimulation or acetylcholine should be decreased. Conversely, as blood pH is decreased with carbon dioxide, hydrochloric acid or lactic acid, acetylcholine is less rapidly hydrolyzed by cholinesterase than it was at normal blood pH. Subsequently, cardioinhibi-

tory effects are enhanced in the presence of an acid blood pH. During vagal stimulation, the endogenous release and cardioinhibitory effect of acetylcholine are dependent on blood pH and particularly the cellular pH of the effector organ, in this case the heart. The pH measurements were made on arterial blood, and critical values for intracellular hydrogen ion concentration in the heart are not known. A qualitative relation may be assumed, but evidence for quantitative differences are real.

Laboratory evidence for potentiation of cardioinhibitory effects during chemical and faradic vagal stimulation have a bearing in surgery. Because vagal stimulation is inadvertently caused by *endotracheal intubation* or *extubation*, when the patient is rather light and reflexes less depressed, occasional cardiac arrests at such times are probably more than coincidental. Operative manipulation in the thorax or abdomen also causes varying degrees of vagal stimulation, especially along the afferent pathways. Under conditions of an acid blood pH, potentiation of such reflexes may prove fatal. Possibly avoidance of acidosis during operative procedures will decrease incidence of cardiac arrest. Many surgeons and anesthesiologists have noted improved cardiac tone and increased cardiac rate associated with active "bagging" of patients undergoing intrapleural surgery, especially when the lungs had previously been inadequately ventilated. The improved cardiac status is probably partly due to correction of hypercapnia and not solely to correction of hypoxia.

**Cardiac Arrest.** A. O. Singleton, Jr., and A. W. DeLoach<sup>7</sup> (Univ. of Texas) stress that the main problem lies in prevention and recognition rather than active treatment, even though this may save some lives. The usual cause of cardiac arrest is anoxia or hypoxia, the latter may be caused or accentuated by anemia, shock or incomplete blood replacement. Overdoses of anesthetics and multiple agents have often been incriminated, but cardiac arrest has occurred with every type of anesthetic, including local and spinal. Cyclopropane, ethyl chloride and chloroform are believed to sensitize the heart directly to epinephrine and thus bring about cardiac arrest. Hypersensitivity to anesthetics is a possible factor in a few cases.

(7) Texas Rep. Biol. & Med. 13:1027-1034, Winter 1955.

Recent experimental and clinical evidence tends to minimize vagal effects as a cause of cardiac standstill. Hyperexcitability has been largely excluded because deaths due to excitement usually occur in individuals with previous cardiac disease. Status thymicolymphaticus, once used to explain sudden operative deaths in children, is no longer considered an etiologic entity.

Reported incidence of cardiac arrest ranges from 1/1 000 to 1/5,000 anesthetics, resulting in 5,000-10,000 deaths/year. It is difficult to know whether incidence is actually increasing, perhaps accentuated by more complex anesthetic and surgical procedures, or whether an increasing number of cases merely reflects better recognition. Cardiac arrest is more common in thoracic operations, 85% of cases occur in the operating room.

Since irreparable damage occurs when the brain is deprived of oxygenated blood for three to four minutes, prompt recognition of failure of heart function is important. Many times the condition is recognized without knowing how long it has existed. Often correction of the cause (overdose of anesthetic or anoxia) will start the heart, but if arrest cannot be ruled out within seconds, the chest must be opened and cardiac massage begun. Forced respirations must be maintained, and an endotracheal tube usually must be inserted if not already in place. Mouth-to-mouth breathing can be used until insertion can be accomplished.

Once oxygenation and massage are established, auxiliary procedures can be carried out. These include intracardial injection of 1 cc of 1:1000 epinephrine solution, pricking the heart with a needle or a blow to the pericardium, injection of 2-4 cc of 10% calcium chloride into the left ventricle, electric stimulation to cause defibrillation, quinidine, procaine amide, potassium chloride, intra-arterial transfusions, Trendelenburg position, intermittent clamping of the aorta, heparin and nor-epinephrine.

Statistics on results of cardiac massage vary. In one large collected series, only 250 of 1,000 lived. In another series of 350 cases, recovery was reported in 112, in 91% of these circulation was restored in less than four minutes. Cardiac standstill occurring outside the operating room is nearly always fatal.

The authors' seven cases all resulted fatally. Five in-

ances occurred in the operating room, one after transferral of the patient to the ward and one during reduction of a fracture under anesthesia in the outpatient department. Cardiac massage was started in all patients within four minutes after cardiac standstill. Heartbeat was restored within 10 minutes after starting massage in four, but they never regained consciousness and died 4 hours to 11 days later. In the others there was no response to massage for about one hour or to cardiac injections. Cardiac arrest apparently was not recognized at the moment it occurred or there had been prolonged anoxia or hypoxia before the heart stopped beating.

[The authors neglect to include asphyxia as a contributing factor. Carbon dioxide retention as well as hypoxia is an important factor.—Ed.]

**Effects of Common Respiratory Phenomena during General Anesthesia on Arterial Blood Pressure and Pulse** were demonstrated on patients and volunteers by Richard E. Jones, Martin Helrich and James E. Eckenhoff<sup>8</sup> (Univ. of Pennsylvania). Normal cyclic changes in blood pressure (which may reach 70 mm Hg systolic) vary from person to person and in the same person under changing circumstances. Experimental and clinical findings indicate that arterial pressure falls when the lungs are inflated. In a patient with bradycardia, deep inspiration caused decline in blood pressure from 100/60 to 78/38. With inspiration, there is an increase in right ventricular output, closely approximating in capacity that of the pulmonary vascular bed. With expiration, this blood is forced into the left heart, cardiac output increases and blood pressure rises.

In the conscious subject, forced expiration against a closed glottis (Valsalva maneuver) causes (1) sharp increase in systolic, diastolic and pulse pressure lasting 1-2 seconds, (2) decrease in systolic, diastolic and pulse pressure becoming maximal in 6-10 seconds, (3) slow return of all three toward control values, (4) with release of pressure, sharp slight decrease in all values and (5) an "overshoot" above control values which reaches a maximum in 4-7 seconds. Modifications of the Valsalva maneuver commonly seen during general anesthesia include coughing, retching, partial airway obstruction and application of positive airway pressure to insure ventilation.

(8) *Anesthesiology* 17:325-333, March 1956.



## ANESTHESIA

Recent experimental and clinical evidence tends to minimize vagal effects as a cause of cardiac standstill. Hyperexcitability has been largely excluded because deaths due to excitement usually occur in individuals with previous cardiac disease. Status thymicolymphaticus, once used to explain sudden operative deaths in children, is no longer considered an etiologic entity.

Reported incidence of cardiac arrest ranges from 1/1,000 to 1/5,000 anesthetics, resulting in 5,000-10,000 deaths/year. It is difficult to know whether incidence is actually increasing, perhaps accentuated by more complex anesthetic and surgical procedures, or whether an increasing number of cases merely reflects better recognition. Cardiac arrest is more common in thoracic operations, 85% of cases occur in the operating room.

Since irreparable damage occurs when the brain is deprived of oxygenated blood for three to four minutes, prompt recognition of failure of heart function is important. Many times the condition is recognized without knowing how long it has existed. Often correction of the cause (overdose of anesthetic or anoxia) will start the heart, but if arrest cannot be ruled out within seconds, the chest must be opened and cardiac massage begun. Forced respirations must be maintained, and an endotracheal tube usually must be inserted if not already in place. Mouth-to-mouth breathing can be used until insertion can be accomplished.

Once oxygenation and massage are established auxiliary procedures can be carried out. These include intracardial injection of 1 cc of 1:1000 epinephrine solution, pricking the heart with a needle or a blow to the pericardium, injection of 2-4 cc of 10% calcium chloride into the left ventricle, electric stimulation to cause defibrillation, quinidine, procaine amide, potassium chloride, intra arterial transfusions, Trendelenburg position, intermittent clamping of the aorta, heparin and nor epinephrine.

Statistics on results of cardiac massage vary. In one large collected series only 250 of 1,000 lived. In another series of 350 cases recovery was reported in 112, in 91% of these circulation was restored in less than four minutes. Cardiac standstill occurring outside the operating room is nearly always fatal.

The author's seven cases all resulted fatally. Five in-

stances occurred in the operating room, one after transferral of the patient to the ward and one during reduction of a fracture under anesthesia in the outpatient department. Cardiac massage was started in all patients within four minutes after cardiac standstill. Heartbeat was restored within 10 minutes after starting massage in four, but they never regained consciousness and died 4 hours to 11 days later. In the others there was no response to massage for about one hour or to cardiac injections. Cardiac arrest apparently was not recognized at the moment it occurred or there had been prolonged anoxia or hypoxia before the heart stopped beating.

► [The authors neglect to include asphyxia as a contributing factor. Carbon dioxide retention as well as hypoxia is an important factor.—Ed.]

**Effects of Common Respiratory Phenomena during General Anesthesia on Arterial Blood Pressure and Pulse** were demonstrated on patients and volunteers by Richard E. Jones, Martin Helrich and James E. Eckenhoff<sup>8</sup> (Univ. of Pennsylvania). Normal cyclic changes in blood pressure (which may reach 70 mm Hg systolic) vary from person to person and in the same person under changing circumstances. Experimental and clinical findings indicate that arterial pressure falls when the lungs are inflated. In a patient with bradycardia, deep inspiration caused decline in blood pressure from 100/60 to 78/38. With inspiration, there is increase in right ventricular output, closely approximating in capacity that of the pulmonary vascular bed. With expiration, this blood is forced into the left heart, cardiac output increases and blood pressure rises.

In the conscious subject, forced expiration against a closed glottis (Valsalva maneuver) causes (1) sharp increase in systolic, diastolic and pulse pressure lasting 12 seconds, (2) decrease in systolic, diastolic and pulse pressure becoming maximal in 6-10 seconds, (3) slow return of all three toward control values, (4) with release of pressure, sharp slight decrease in all values and (5) an "overshoot" above control values which reaches a maximum in 4-7 seconds. Modifications of the Valsalva maneuver commonly seen during general anesthesia include coughing, retching, partial airway obstruction and application of positive airway pressure to insure ventilation.

(8) *Anesthesiology* 17:325-333, March 1956.

If positive airway pressure is maintained for more than a few seconds, a proportion of the applied pressure is absorbed by the elasticity of the lungs, but the remainder is transmitted to the pulmonary vasculature, the great veins and the heart. To preserve blood flow to the right heart and from the right to the left heart, pressure within these vessels must increase to compensate for raised intrapulmonary pressure. If this adjustment fails, cardiac output and arterial pressure fall in proportion to increased pressure. If intermittent positive pressure is substituted for continuous positive pressure, fall in blood pressure may be obviated or minimized.

Shorter, more explosive rise and fluctuations of blood pressure may be of less concern than longer periods of hypotension with maintained elevation in airway pressure, but in an elderly patient, sudden rises may cause cerebral hemorrhage, and, in one with poor myocardial reserve, may lead to sharp reduction in blood supply and myocardial infarction. In both situations, sharp decline of blood pressure after the upward spike may be the dangerous factor. In patients with auricular fibrillation or history of embolism, these violent changes may cause further embolic phenomena. Occasional cardiac arrest following aspiration of tracheal secretions may be connected intimately with sudden elevations in blood pressure due to brief increases in airway pressure.

Fortunately, most patients are able to compensate for increases in airway pressure by peripheral vasoconstriction and elevation in central venous pressure, but occasionally compensation fails to occur. Patients made apneic by injudicious use of anesthetic or relaxant drugs may be unable to return to spontaneous respiratory movements at ambient pressures and the outcome may be disastrous. That death may occur at operation or hours to days later from myocardial damage due to prolonged hypotension during anesthesia comprises the principal reason for avoiding rapid techniques of inducing anesthesia in all but good risk patients.

The relation to morbidity or mortality of respiratory complications observed during and after administration of anesthetics is rarely clearcut. However, an awareness of the mechanisms by which complications influence the circulation is important in understanding the fundamental principles of anesthesiology.

**Hemodynamic Studies during Thiopental Sodium and Nitrous Oxide Anesthesia in Humans** E J Fieldman, Roger W Ridley and Earl H Wood<sup>9</sup> (Mayo Clinic and Found) studied hemodynamic variables, correlating changes with depth and duration of anesthesia, in 13 patients with normal cardiovascular status. EEGs determined anesthetic levels.

The cardiac index of all patients showed a mean decrease of 24% with EEG anesthetic levels of 1 and 2 and further decreased by 24% of these values when anesthesia was deepened to levels 3, 4 and 5 (burst suppression levels). On return to lighter levels cardiac index did not increase in 25 minutes. There was a mean decrease in stroke index of 27% at anesthetic levels 1 and 2 and a further 24% decrease at levels 3-6. On return to lighter levels, there was a mean increase of 18%.

At lighter anesthetic levels, mean arterial blood pressure fell 19%, with no further change at deeper levels. Decrease in systolic pressure was 23% with rapid induction and 8% with slow induction, (2 cc/minute), the fall being greatest in patients with the highest mean pressure before induction. There were no significant changes in cardiac rate. Central blood volume decreased with deepening anesthesia and peripheral resistance increased. Central venous pressure increased during induction and decreased at levels 3-5, but changes were equivocal suggesting that myocardial sufficiency was maintained. The decrease in cardiac index with parallel decrease in "central blood volume" and the decrease in blood pressure with no change in peripheral resistance in light anesthesia suggest vasodilatation with peripheral pooling and decrease in venous return to the heart.

Arterial blood pH decreased with deepening anesthesia unless respirations were assisted. Carbon dioxide retention at deeper levels may affect blood pressure and peripheral resistance, to decrease cardiac output further. Just before production of apnea respiratory frequency increased significantly. Arterial O<sub>2</sub> saturation fell with induction when the patient was breathing room air and rose again when the N<sub>2</sub>O-O<sub>2</sub> mixture was added. In patients given 100% oxygen for eight minutes before induction there was no decrease. There were no ECG changes in 12 of 13 patients.

(9) *Anesthesiology* 16:473-489 July 1955

## MISCELLANEOUS

**Alevaire® Adjunct for Preventing Pulmonary Complications after Thoracotomy Comparative Study of 200 Cases** is reported by J Eugene Ruben, William Jamison and K V S Rao<sup>1</sup> (Philadelphia) The patients had had successful thoracotomy for cardiac pulmonary or other intrapleural operations In 82 patients, alevaire® a respiratory detergent in nebulized continuous oxygen administration through a nasopharyngeal catheter was given for the first 48 postoperative hours Less than 500 cc alevaire® was used in the average case The other 118 patients had continuous humidified oxygen therapy by the same route There was no other variant in postoperative management

In patients given alevaire®, incidence of parenchymal pulmonary complications, demonstrated by changes in postoperative chest films, was 11%, in those given humidified oxygen, 23.6% Incidence of bronchoscopy was 7% in the former group and 13.5% in the latter Thus the two tabulated incidences of pulmonary difficulty were twice as frequent in the nontreated group and further use of alevaire® seems justified

► [Although not indicated in the abstract the patients who did not receive the detergent were operated on before 1953 whereas those receiving the detergent were operated on after 1953 Since a number of other factors could have influenced these two groups it is difficult to accept the results It is also difficult to conceive that no other variant in postoperative management developed over a six year period in a field in which improvements in management have occurred almost yearly—Ed]

**Mechanism Involved in Anesthetic State** Electrical excitation of a primary sensory system is appreciated as a perception in an alert individual Potentials however can be recorded in these primary systems during anesthesia J D French and F E King<sup>2</sup> (Long Beach, Calif) investigated the reticular system of the brain in search of a second afferent system functioning as a reticular activating system (RAS) that might be blocked during anesthesia Collateral fibers from all primary pathways enter the RAS, and neuronal systems diffuse from it over the entire cortex A single peripheral stimulus can be recorded in the RAS as well

(1) *Anesthesiology* 16:801-804 September 1955

(2) *Surgery* 38:228-238 July 1955

as in the primary systems, and if applied in a sleeping animal, will give electrical and behavioral response of wakefulness. Figure 156 shows that the RAS potentials from a single shock to the sciatic nerve are blocked by ether or barbiturates, whereas the potential in the medial lemniscus persists. Likewise, stimulation of the RAS ordinarily causing

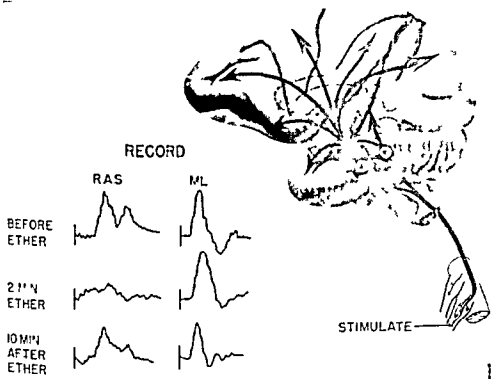


Fig 156—Tracings from oscilloscope records on left show effect of ether anesthesia on potentials evoked simultaneously in direct sensory pathways (ML—medial lemniscus) and RAS from single shock stimulation of sciatic nerve. Note that potential elicited in RAS disappears after two minutes of ether application but returns when anesthetic has been removed. Contrastingly anesthesia has no effect on potentials evoked in medial lemniscus. (Courtesy of French J D and King E E. *Surgery* 38:228-238, July, 1955.)

arousal will not change the EEG during anesthesia. Both these effects of anesthesia are reversible.

Electrocoagulative destruction of the RAS produces coma even though stimuli continue to be conducted through the long motor and sensory pathways, resembling the reversible changes induced by anesthesia. Postmortem studies of human beings who had been in coma from brain disease and injury, who behaved like these experimental animals, showed destruction of neurons in the arousal mechanism system of the RAS or its corticopetal reflections.

**Influence of Various Anesthetics and of Ammonium Chloride on Disappearance of Procaine from Plasma in the Intact Dog** Previous studies of effects of anesthesia on the disposition of procaine have not included cyclopropane, with which local anesthetics often are used clinically, or pentobarbital sodium, the commonest laboratory anesthetic, nor have they afforded a comparison of anesthetized and unanesthetized states in the same animal or study. The effect of acidity on concentration of procaine in the plasma of the intact animal has not been recorded.

C W White, Jr, and E D Swiss<sup>3</sup> (Boston Univ) studied the disappearance of procaine from plasma of dogs following rapid intravenous injection of single doses during anesthesia with various agents. Effect of ammonium chloride on plasma procaine during pentobarbital sodium anesthesia was also considered. Ether and chloroform anesthesia were associated with high concentrations of procaine in the plasma, cyclopropane occupied an intermediate position, and barbiturate anesthesia was characterized by lower concentrations, similar to those in unanesthetized animals. Apparent volume of distribution of procaine was lower during cyclopropane and ether anesthetics than in unanesthetized dogs.

Rate of disposition of procaine was increased during pentobarbital anesthesia and was higher with cyclopropane than with ether or chloroform. Agents which increase the apparent volume of distribution and rate of disposition are favorable for use with procaine. Of the drugs studied, pentobarbital sodium seems the most favorable and ether the least so on this basis, agreeing with findings of other workers who used different methods.

The sudden significant rise in procaine concentration in plasma following injection of ammonium chloride indicates that procaine may be bound in the body in some combination sensitive to changes of pH. Higher procaine levels in a more acid situation suggest an explanation for elevation of procaine concentrations during anesthesia. The transient quality of increase in procaine concentration is probably the result of rapid adjustment of acid base balance.

**Treatment of Adrenal Cortical Insufficiency during Surgical Procedures** is reported in seven cases by William S

Howland, Olga Schweizer, C Paul Boyan and Alma C Dotto<sup>1</sup> The increasing number of radical surgical procedures performed on chronically ill patients and the frequency of cortisone therapy for various conditions result in greater incidence of adrenocortical insufficiency during surgery. In one year at the Memorial Center for Cancer, 1 of every 300 surgical patients showed some form of hypofunction of the adrenal cortex during surgery or in the immediate postoperative period.

Persistent hypotension during surgery, with failure to respond to adequate blood replacement and vasoconstrictors, respiratory depression and a prolonged reaction time after anesthesia, are interpreted as the manifestation of adrenocortical insufficiency. In this category can be grouped cases formerly classified as irreversible shock or anesthetic shock. Adrenocortical insufficiency is to be expected in patients who have been chronically ill, who have disease involving the adrenals or who have had adrenalectomy.

The logical treatment, if the condition develops during surgery, is intravenous administration of hydrocortisone, the steroid of choice because of its rapid action. It is commercially available in the form of 100 mg hydrocortisone dissolved in 200 cc of 50% ethanol. For intravenous administration, it must be diluted in 500 cc saline or 5% dextrose in water to eliminate the irritating effect of concentrated ethanol. Its effects were strikingly exemplified in the authors' seven patients who were enfeebled by severe illness or predisposed to irreversible shock for other reasons. Patients with blood pressure too low to measure and with pulse impossible to count responded promptly to hydrocortisone and recovered from anesthesia without further difficulty. The results suggest that the basic physiologic disturbance was deficiency of adrenocortical secretion. The exact mechanism by which hydrocortisone produces elevation of blood pressure and reversal of the shock state is unknown.

► [Although there is evidence, and perhaps this article is a part of it, that patients can benefit from hydrocortisone, one must be careful to avoid using this preparation as a panacea. Persistent hypotension may be due to many factors, all of which must be given serious consideration before and in conjunction with the use of hydrocortisone. In the absence of objective measurements, determination of "adequate" blood replacement is subject to gross error. Hypoventilation and prolonged reaction time are



often due to mismanagement of anesthesia and do not necessarily reflect deficiency in adrenal output of steroids—Ed ]

**Hypnotism and the Anesthetist.** Anthony Owen-Flood<sup>5</sup> (London) points out that the stigma of the side show still attached to hypnosis has prevented the physician-anesthetist from using this method of reducing pre- and postoperative tension and of relieving pain. The hypnotic state induced by thiopentone can serve as the primary induction into true hypnosis, then achieved by the anesthetist's stream of suggestive words. This is 100% effective. The posthypnotic suggestion that at a given signal this state can be achieved again, without thiopental, will be effective and subsequent induction easy. Hypnosis can effectively lessen preoperative anxiety, is ideal and safe as sedation and can minimize the attendant increased anesthetic and surgical risk of the tense patient. Posthypnotic suggestion reduces postoperative tension and can reduce excessive vomiting. In children, hypnosis can often be achieved easily without drugs, or with the use of nitrous oxide or ethyl chloride vapors blown into the face from a tube hidden in the operator's hand.

Nowhere is hypnosis used to better advantage than in childbirth. Hypnotic conduct of labor produces muscle and psychic relaxation, yields control of abdominal and levator ani muscles to the hypnotist and allows painless and safe labor and delivery. Hypnosis was used effectively by the author in epilepsy, in which the aim was decrease in number of attacks and inducing attacks to occur during the night rather than the day. Hypnosis was also effective in autoeroticism, somnambulism and nocturnal enuresis. Hypnosis during laparotomy induced fair relaxation. Pain was absent and the postoperative course comfortable. It does not prevent postoperative shock, which occurred in the laparotomy patient and responded to morphine.

**Surgery under Hypnosis** is discussed by A. A. Mason<sup>6</sup> (West London Hosp.), with report of a patient who successfully underwent dental surgery and then second stage mammoplasty. It is important to define the area of suggested anesthesia accurately and extensively enough. With hypnosis, there are none of the toxic side effects of chemical anesthetics, and shock is minimized. It may thus be of use in severely ill patients when chemical anesthesia is con-

(5) *Brit. J. Anaesth.* 27: 398-404, August, 1955

(6) *Anaesthesia* 10: 295-299, July, 1955

tranquillized. Hypnotic anesthesia is used to best advantage in obstetrics, providing prolonged, nontoxic analgesia and freedom from anxiety in labor, yet permitting contractions to continue and the mother to be conscious at the time of birth. Protective reflexes are retained, except those specifically rendered negative, hence such accidents as burns, nerve palsies and aspiration are less likely to occur. Repeated procedures, e.g., burn dressings, are done to great advantage under hypnosis. Postoperative vomiting and pain can be eliminated by posthypnotic suggestion.

Uncertainty of result is the major disadvantage of hypnosis. Not over 25% of patients could be operated on by this method, and it is impossible to forecast suitable subjects. Testing and conditioning of patients to obtain desirable operative conditions is time consuming.

► [The use of hypnosis as the sole anesthetic is dramatic, but limited in its application. However use of hypnotic technics as adjuncts to standard anesthetic technics has much merit and more anesthesiologists should exploit suggestion in the management of anesthetic problems.—Ed.]

**Inhibition of Acid-Induced Peptic Ulcer Pain by Local Anesthetics.** Edward R. Woodward and Herbert Schapiro<sup>7</sup> (Los Angeles) report a study on patients with active but uncomplicated peptic ulcers. Multilumen tubes were placed in the pyloric antrum and duodenum under fluoroscopic control. In one patient with gastric and four with duodenal ulcer, direct infusion of N/10 HCl was promptly followed by onset of characteristic ulcer distress. Direct application of topical anesthetic agents—xylocaine<sup>®</sup>, pontocaine<sup>®</sup> or nupercaine<sup>®</sup>—into the region of the peptic ulcer crater completely blocked the pain response to HCl in three and markedly reduced the response in two. Introduction of the local anesthetics into either or both stomach and duodenum had no effect on motility of the organs, making it unlikely that inhibition of ulcer pain was the result of effects on motility. No recordings were made of pyloric sphincter tone. The most convincing explanation is that when nerve endings within the ulcerated area were anesthetized, pain response to acid irritation was blocked. The findings support Palmer's hypothesis that afferent nerve endings in an ulcer crater can be stimulated by chemical means.

Recent Advances in Neurophysiology of Pain are dis-

with peripheral vascular diseases who fail to respond to lumbar sympathetic nerve block

There are definite advantages of this test for sympathetic activity (1) The test is entirely independent of environmental temperature and does not require equilibration of the patient to attain a stable state (2) No special equipment is required (3) A permanent record is obtained (4) The test is rapid and requires little training of personnel (5) It indicates definitely whether chemical or surgical sympathetic nerve block has been obtained, and does not depend on a satisfactory response to block

If it can be established by use of this test that complete sympathetic nerve block has been accomplished, clinical response

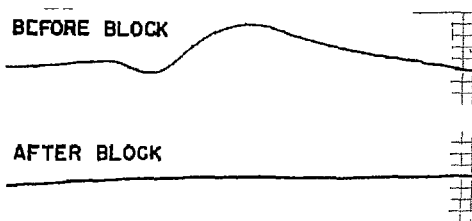


Fig 157—SGR evaluation of right lumbar sympathetic block using 10 cc of pontocaine® standard ECG tracing at 25 mm/second (Courtesy of Lewis L. Anesth & Analg 34 334 345 Nov Dec 1955)

then be evaluated to determine the probable result of surgical sympathectomy. Therapeutic nerve block using phenol can be used in patients with acute thrombophlebitis to prevent cast splitting in a postoperative orthopedic case or in numerous conditions in which sympathectomy lasting a month or two would be adequate. In peripheral vascular diseases or pain problems that may require permanent sympathectomy, 6% phenol nerve block must be considered a diagnostic procedure.

The test in itself will not prognosticate the efficacy of surgical sympathectomy, but when combined with assessment of vascular function, it provides an intelligent approach to clinical evaluation. The SGR has also proved of value

diagnosis of certain neurologic lesions, in evaluating effect of and dose response to drugs that affect the sympathetic nervous system and in measuring completeness of surgical sympathectomy

**Postanesthetic Nausea, Vomiting and Retching Evaluation of the Antiemetic Drugs Dimenhydrinate (Dramamine<sup>®</sup>), Chlorpromazine and Pentobarbital Sodium** M Robert Knapp and Henry K Beecher<sup>1</sup> (Harvard Med School) report a controlled study on 554 patients after nitrous oxide-ether anesthesia. Effective reduction in postoperative nausea, vomiting and retching during the first four postoperative hours was produced with 50 mg chlorpromazine and with 150 mg pentobarbital. Chlorpromazine protected the patient for 24 hours. Disadvantages were increase in awakening time, hypotension of serious degree and, with pentobarbital, considerable confusion and excitement.

Dimenhydrinate or pentobarbital in 100 mg dosage failed to prevent the symptoms. Analysis of placebo data showed no significant differences in degree of postoperative symptoms when the site of operation was categorized as intra peritoneal or extraperitoneal.

When a patient with a gastric tube in place receives 150 mg pentobarbital, he derives considerable protection against emetic symptoms. Those given the placebo, dimenhydrinate or chlorpromazine showed no differences in incidence of symptoms when a gastric tube was present. Females have significantly more postoperative nausea, vomiting and retching than males, once the initial four postoperative hours have passed. Age does not influence incidence of symptoms, but antiemetics seem most helpful to patients over age 40.

Only 6.5% of the patients studied were dissatisfied with nitrous oxide ether anesthesia. The authors conclude that at present it is probably unwise to adopt therapy with pentobarbital (150 mg) and chlorpromazine (50 mg) routinely as prophylaxis against postoperative nausea, vomiting and retching because of depressant and hypotensive effects.

**Subjective Response and Reaction to Sensation** Reaction Phase as Effective Site for Drug Action is documented by numerous studies discussed by Henry K Beecher<sup>2</sup> (Har-

(1) JAMA 160:376-385 Feb 4 1956  
(2) Am J Med 20:107-113 January 1956

vard Med School) In 1895, Marshall and Strong speculated as to the existence and importance of the reaction or processing, component in suffering It is assumed that all pain experience in man consists of the original sensation plus psychic reaction to that stimulus, and that in various situations there are great quantitative differences in the role of each component Importance of the assumption hinges on the question of how great the reaction element actually is

Severe wounds with great significance and presumably great reaction are made painless by small doses of morphine, whereas fleeting experimental pains with no serious significance are not blocked by morphine The difference seems to be in the difference of significance of the two wounds Morphine acts only on significant pain

The total situation greatly influences the reaction that develops in it After removal from battle badly wounded men were often euphoric reaction to wounds and to the relative safety of the forward hospital was one of happiness About 75% of the wounded, in good general condition, denied pain from extensive wounds or had so little pain they wanted no medication In a group of male civilians who suffered far less tissue trauma from major surgery, only about 20% wanted no analgesic medication These data show that there is no simple direct relation between the wound per se and pain experienced Pain is largely determined by other factors and reaction to the wound is highly important In man experimental pain has proved useless in appraising analgesic power but pathologic pain is highly useful In both man and animal narcotics are effective but chiefly probably only in the presence of significant meaning of pain involved, i.e. subjective reaction to it

Most soldiers who do not complain of grievous wounds complain as vigorously as others at an inept venipuncture, indicating that there is no total pain block It is difficult to understand how emotion can affect the basic pain apparatus other than by affecting the reaction to the original sensation

Other evidence supporting the view that the most important factor in suffering is the reaction was found in patients' differentiation between comfort and pain relief after morphine and phenobarbital Of 143 postoperative patients receiving 8 mg morphine/70 kg intravenously, 27 had

neither comfort nor pain relief, 7 had pain relief but no comfort, 9 had comfort but no pain relief and 100 obtained both comfort and pain relief. The latter two categories represented the desired therapeutic effect. After intravenous injection of 60 or 90 mg pentobarbital sodium/70 kg in 146 patients, 5 had pain relief without comfort and 16 comfort without pain relief. Presumably "comfort" is established by the reaction. Comfort and pain relief can be separated by a barbiturate, by morphine and by prefrontal lobotomy. With apparently persisting pain ("my pain is the same, but it doesn't hurt me now"), comfort can be established by blocking certain nerve impulses.

Even stronger support for the importance of reaction in suffering is furnished by repeated demonstration of relief attained with placebos. Placebo effect averaged 35% in numerous studies. Since only about 75% of patients in severe pain can be satisfactorily relieved by even large doses of morphine, placebo effect amounts to about 50% of drug effectiveness. Placebos, being organically ineffective, can only effect reaction. When postoperative wound pain was greatest, morphine relieved 52% of one group and placebo relieved 40%. Half were given morphine first and then a placebo, the order was reversed in the other half. The increased effectiveness of placebos with increased stress can seemingly only be explained by the importance of the reaction or processing component of suffering.

# INDEX

## A

- Acne scars, rotary abrasive techniques for removal of, 108
- Adenoma *bronchial*, 186, —with liver metastasis, 188
- Adenomatosis *pulmonary*, 216
- Adhesions inhibitory effects of hydrocortisone acetate on, 335; plasmin in prevention of, 336
- Adrenal cortex autograft (human) into portal circulation, 506, function in combat casualty, 507, hyperfunction, blood and urinary electrolytes in, 508, insufficiency during surgery, 618
- Adrenalectomy *bilateral*, in advanced breast carcinoma, 502 ff
- Afferent loop syndrome after Billroth II gastrectomy, 447
- Aged appendicitis in, 463, breast cancer in, 158, intestinal obstruction in, 460
- Aldosterone increased excretion after operation, 27
- Aleaire® for prevention of pulmonary complications after thoracotomy, 616
- n-Allylnormorphine effect on pethidine-induced rise in CSF pressure, 545
- Amputation *interilio-abdominal*, 535 refrigeration for, 519
- Anastomosis *arterial*, end-to-side technique, 314, *left-sided bronchotracheal*, 184 *portacaval*, rationale and indications, 351
- Androgens induced exacerbation of breast cancer measured by calcium excretion, 151, therapy in metastatic breast cancer, 150
- Anesthesia antiemetic drugs for prevention of nausea, vomiting and retching after, 625, blood volume studies using radiochromium 51, application to anesthesiology, 603 EEG patterns during steroid and barbiturate narcosis, 577 *endotracheal*, for tonsillectomy in children, 571, *general*, denitrogenation with nonbreathing, semiclosed inhaler and circle systems, 569, —effects of common respiratory phenomena on arterial blood flow and pulse during, 613; —nitrogen elimination with semiclosed inhalers, 570; —relation between hemodynamics and plasma volume alterations during, 601; *local*, deaths from, 589; —inhibition of acid-induced peptic ulcer pain by, 621, —in newborn, 591, —new method for peroral endoscopy, 592, —for pain in peripheral arterial ischemia, 592; lung function tests for evaluation of anesthetic risk, 565; mechanisms in, 616, *spinal* effect of resulting hypotension on coronary blood flow and myocardial metabolism in man, 587, —headache after, treatment, 587, —neurologic complications, 580 ff
- Anesthetic agents (see also specific drugs) effects on vascular tone, using Sandison-Clark chambers, 607
- Aneurysm *arteriovenous*, of pulmonary vessels, 246
- Angina pectoris de-epicardialization for, 254
- Angiocardiography reduced intrathoracic circulation as aid in, 258
- Angiography *cerebral*, circulatory disturbances during, 599, *thoracic*, in bronchial carcinoma, 211
- Anoxia diffusion, with anesthesia, 561
- Anticoagulants uses and contraindications for, 50
- Antrenyl® for anticholinergic effect in preanesthetic medication, 542
- Anuria and uremia, treatment of surgical patients with 24
- Aorta coarctation, controlled hypotension during, surgery for, 294, *defects*, cross-turned autogenous arterial grafts for, 304, —vena cava autografts for, 305, *stenosis*, diagnosis of, 288, —evaluation by left heart catheterization, 269 *terminal*, occlusive disease of, 319

- Appendicitis acute, with cecal cancer, 478; in aged, 463; diminishing mortality from, 461, and ileus, 462
- Appendix normal, 465; vermiform, study of specimens (human), 464
- Arachnoiditis adhesive, and vascular blockage caused by detergents, experimental study, 582
- Arteries coronary, disease operative risk in patients with 23, —surgery for disease of, 247 ff; injuries from firearms, conservative treatment of, 292, mammary (internal), implantation into left ventricular myocardium for coronary artery disease, 249, pulmonary, arteriovenous aneurysm of, 246, —blood flow with controlled respiration, 554
- Arteriosclerosis occlusive, femoral, endarterectomy in (semiclosed technic), 302, —of legs, by pass operation for, 511
- Arthritis rheumatoid of hand, surgery of 522
- Automobile accidents prevention of injuries and deaths from, 9
- B**
- Banti's syndrome surgery for, 352 ff
- Beck operation for coronary artery disease, 247, 251 ff
- Bile ducts atresia (congenital), cholecystojejunostomy for, 380, strictures of, treatment, 374
- Biliary tract (see also Gallbladder) drainage after choledochostomy, 373, erythromycin excretion through, 362 surgery (1954 review from Mayo Clinic), 377
- Biopsy of rectum in ulcerative colitis, 477, safety in cancer (?), 87
- Blood "arterialized" for determination of arterial O<sub>2</sub> and CO<sub>2</sub> tensions, 48, changes, in hypothermia 595, flow, coronary, effect of hypotension due to spinal anesthesia on 587, loss, and operative time, with and without controlled hypotension 32, reaction of serous cavities to, 38, transfusion (see Transfusions), volume determinations, with radioactive iodinated serum albumin, 603; —using radiochromium 51, 603
- Blood vessels (see also specific vessels) replacement, 307 ff
- Bones long, fractures (ununited), massive sliding inlay bone grafts for, 531, tumors, giant cell (benign and malignant), 534
- Breast cancer 133 ff, —in aged, treatment, 158, —androgen induced exacerbation of measured by urinary calcium, 151, —bilateral adrenalectomy in, 502 ff, —castration for, 159, —endocrine insufficiency after hypophysectomy in patients with, 154, —endocrine therapy in 148 ff, —evaluation of McWhirter treatment, 140, —fundamental concepts determining treatment in, 155, —hereditary factor in, 147, —hypophysectomy in, 148 ff, 152, —inflammatory, critique of therapy, 159, —limitations in diagnosis and treatment, 143; —in male, 135, —other breast, 133, —preoperative x-ray therapy in high doses followed by radical surgery for, 134, —significance of parasternal glands in, 145, —surgical results at Johns Hopkins Hospital, 142, plastic surgery, Ivalon sponge prosthesis in, 138, thrombophlebitis of superficial veins of, and anterior chest wall, 324, traumatic fat necrosis of, 18
- Bronchiectasis indications for surgery in, 169, prognosis after surgical resection 170, a surgical disease (?), 167
- Bronchography bilateral, new material and technic, 166
- Bronchspirometry for measurement of maximal breathing capacity in individual lungs, 163
- Bronchus adenoma, with liver metastasis, 188, —treatment of, 186, carcinoma (see also Lungs), —bronchoscopy, bronchography and angiopneumonography in, critical comparison, 210, —combined radiotherapy and resection for, 202, —induction by local massive carcinogen in outdrifting mucus, 194, —natural duration of, 214, —pneumonectomy (radical) for, 205, —thoracic angiography 211, —tuberculous lesions



ciated with, 223, fistulas, endoscopic treatment of, 172, left lower lobe, and trachea, anastomosis of, 184

Burns in children, treatment of, 77, corrosive, of esophagus, management of, 414, parenteral fluid therapy for (in first 48 hours), 64, thermal, toxic factor(s) in (experimental), 42

## C

Cancer (see also specific neoplasms and sites) in adults before mid-life, 97, advanced, hypophysectomy in, 152, antiemetic effect of chlorpromazine in advanced disease, 99, biophysical effects of ultrasonic energy on, 107; cachexia, tube feeding in, 55, diagnosis, by bone marrow smears, 83, environmental causes of, 94; multiple primary, case report of four in succession, 91, oil granuloma of therapeutic origin simulating, 90, pain relief in, 100, radiogold for effusions due to, 107, relation of nucleic acid anabolism to treatment of, 104; safety of biopsy in (?), 87, Schultz Dale test for detection of specific antigen in serums of patients with, 85, treatment time and prognosis, relation between, 86, in United States, epidemiology of, 81

Carbon dioxide absorption, practical aspects of, 560

Castration for breast cancer, re-examination of problem, 159

Cecum cancer, with acute appendicitis, 478

Cerebrospinal fluid pressure antidotal effect of levallorphan and n-allylnormorphine on pethidine-induced rise in, 545, increase induced by morphine, 543

Chest funnel, surgical management of, 233

Children burn therapy in, 77, gangrene of extremities as complication of intravenous therapy, 513, respiration, under anesthesia, 564 right lobectomy of liver in, 342, thyroid carcinoma in, 115, 125

Chlorpromazine antiemetic effect in cancer patients, 99, in labor, 539 f; pretreatment, beneficial

action on survival after graded hemorrhage (in rat), 604, for prevention of postanesthetic emetic symptoms, 625

Cholangiography intravenous, in cholecystectomized patients with upper abdominal symptoms, 365, and pancreatography for operative visualization of pancreatic disease, 388

Cholecystectomy complaints after, 370 ff, favorable effects on co-existing heart or coronary disease, 382

Cholecystitis, acute evaluation of early operation in, 367, serum amylase concentration in, 363

Cholecystography during and after acute pancreatitis, 364, reliability of, 363

Cholecystojejunostomy for congenital atresia of bile ducts, 380

Choledochostomy bile drainage after, 373

Circulation disturbances of, during cerebral angiography, 599

Coccidioidomycosis pulmonary, surgery for, 218, surgical aspects of, 41

Colectomy bowel function after, 470, total, in ulcerative colitis, 475

Colitis, ulcerative biopsy of rectum in, 477, colectomy (total) for, 475, cortisone in 476, surgical indications in, 473

Colon carcinoma, right side, resectability and survival rates, 481, —resection (technic), with results, 480, diverticulitis, surgery for, 472, 489, neomycin-nystatin for preoperative preparation of, 80, right for intra-thoracic transplantation in esophageal reconstruction, 406

Colostomy wet, with pelvic extenteration (total), urinary tract after, 510

Coma episodic, due to meat intoxication as fatal complication of portacaval shunt, 57

Commissurotomy, mitral discrepancies between subjective and objective responses to, 280, experience in 400 cases, 279; follow up of 5 years or more, 276, indications, technic and prognosis for, 272

Corticotropin for control of func-

- tioning metastases from islet cell tumor of pancreas, 394  
 Cortisone injurious effects on destructive inflammation, 35, in metastatic breast cancer, 150, in ulcerative colitis, 476  
 Crohn's disease cecal forms, 471  
 Cushing's syndrome blood and urinary electrolytes in, 508  
 Cysts, pilonidal 493  
 Cytology bone marrow smears for cancer diagnosis, 83, in diagnosis of gastric carcinoma, using chymotrypsin lavage, 435 ff, and histopathologic study in lung carcinoma, correlation, 190

## D

- Decortication of lung in tuberculous disease, 178  
 De epicardialization with phenol, for angina pectoris, 254  
 Dextran of different molecular weights, efficacy in shock secondary to limb clamping, 69, inhibition of prothrombin activation with, 68  
 Diabetes foot lesions in, 515  
 Diaphragm eventration of 227  
 Diverticulitis of colon, 489, —surgery for, 472  
 Drugs action, reaction phase as effective site for, 625, analgesic, method of comparing, 537, anticholinergic, in preanesthetic medication, 542, depressant 537 ff  
 Dubost dilator for commissurotomy in mitral stenosis, 273  
 Ductus arteriosus *patent*, postoperative review, 239 —simplified technic for division and suture of, 236, —surgery of, 234  
 Duodenum (see also Ulcer, peptic) primary malignant neoplasms of, 446

## E

- Electroencephalogram patterns during steroid and barbiturate narcosis, comparison, 577  
 Electrolytes blood and urinary, in Cushing's syndrome, 508  
 Electrotherapy convulsive and subconvulsive, during respiratory emergencies in anesthesia, 578  
 Embolism fat, etiology of, 19  
 Empyema pleural, biochemical decortication with hyaluronidase in, 225; *tuberculous*, decortication

- for, 178, —treatment of, 180  
 Endarterectomy semiclosed technic, in obstructive femoral arteriosclerosis, 302  
 Endoscopy peroral, new method of local anesthesia for, 592  
 Endotracheal tube sizes for infants and children, 568  
 Enteritis, regional Brunner type glands in, 459  
 Enterocolitis postoperative pseudomembranous due to staphylococcus 458  
 Esophagus atresia early diagnosis and treatment, 397, benign muscle wall tumors of, 403; carcinoma, 10 year study of, 404, gastroesophageal "sphincter" and mechanism of regurgitation 399, hiatal hernia (see Hernia), intra thoracic transplantation of right colon for reconstruction of, 406, spontaneous rupture of, 400 ff, *stenosis, corrosive*, management of, 414, —supra aortic esophago-gastric anastomosis without resection for, 415, *varices bleeding*, in diagnosis of portal hypertension, 349, —surgical treatment of, 411, varix pressure before and after shunting operations for portal hypertension, 345, weblike lesion in lower third of, 409  
 Estrogens in postmenopausal women with metastatic breast cancer, 150  
 Ether hemodynamic effects of, 600  
 Exsufflation with negative pressure for clearing bronchial secretions postoperatively, 558  
 Extremities (see also Feet, Hands and Legs) gangrene in infants after intravenous therapy, 513

## F

- Fat embolism, etiology of, 19, necrosis, traumatic, 18  
 Feet diabetic, surgical lesions of, 515  
 Fingers tendons, suture of, 524  
 Fistulas bronchial endoscopic treatment of, 172, of thoracic duct, surgical management of, 332  
 Fluid therapy parenteral, of burns, in first 48 hours, 64  
 Foreign bodies penetrating and swallowed, management of, 16  
 Fractures dorsal acetabular, of

- hip, 529, ununited, of long bones, massive sliding inlay bone graft for, 531
- Frostbite experimental, effect of delayed warming on, 520, therapy for, 518
- Frozen section for diagnosis during surgery, 88 f
- G
- Gallamine triethiodide relaxant action of (experimental), 573
- Gallbladder carcinoma, primary, 379, —experimental induction of, 380, —total right hepatic lobectomy for, 340 f
- Gangrene of extremities of infants after intravenous therapy, 513
- Gastrectomy abdominothoracic total, for gastric carcinoma, 440, Billroth II, afferent loop syndrome after, 447, modified radical for stomach carcinoma, 441; tuberculosis after, 449
- Glomus tumors case analysis, 532
- Goiter posterior mediastinal, surgical removal of 129
- Grafts arterial chemically treated Nylon tubes as 300, —cross-turned autogenous for aortic bridge (in dog), 304 —freeze-dry processing of 313, —homografts, chemical modification of, 298, —and venous practical considerations in surgery, 314, bone, massive sliding inlay, for ununited fractures of long bones, 531, free tendon for repair of flexor tendons of hand 526, plastic mesh tube arteriogenesis induced by, 311 synthetic materials for vascular substitutes, 307 ff, vena cava (autografts) for aortic defects 305
- Granuloma oil (therapeutic), simulating cancer, 90
- H
- Hands rheumatic, surgery of 522, tendons, flexor, repair of, 526
- Headache after spinal anesthesia treatment of, 587
- Heart (see also Mitral valve) arrest, causes of, 611 —elective (experimental), 261 f, —external electric pacemaker in, 608, —hypothermic, role of hypoxia in (heart-lung preparation), 594; —operating room deaths from, 259, —primary, experiences with, 260, chambers, digital exploration and mitral murmurs, 283, congenital anomalies, controlled cross circulation for direct surgery for, 264, disease, favorable effects of cholecystectomy on 382, hypothermia in surgery of 242 ff, interatrial septal defects direct suture during hypothermia 243, —surgical closure by circumclusion, 268, left side, hemodynamics of, 256, operations and pregnancy, 291, perfusion for longer periods of cardiac occlusion during hypothermia, 242, surgery, direct controlled circulation in, 263 ff, tricuspid atresia diagnosis and treatment of 286, vagal inhibition, effect of pH changes on 610, ventricular septal defects, controlled cross circulation for direct surgery on 264 ff, wounds, long term follow up, 241, —penetrating treatment of, 240
- Hemangioma capillary, treatment of, 39
- Hemodynamics effects of ether anesthesia 600, of left heart with reference to mitral stenosis, 256, and metabolic interrelations in activity of epinephrine norepinephrine and thyroid hormones 605, and plasma volume alterations, relation between during general anesthesia 601, during thiopental and nitrous oxide anesthesia, 615
- Hemoglobin total, determination in evaluation of blood transfusions in surgical patients, 22
- Hemorrhage massive, general hypothermia in treatment of 28, gastrointestinal causes and treatment of, 420 ff, graded (in rat), beneficial action of chlorpromazine pretreatment on survival after, 604
- Hemorrhoids St. Mark's Hospital (London) operation for, 466
- Hepatitis from blood transfusions 69
- Hernia giant, pneumoperitoneum in 500, hiatal, incidence, diagnosis and treatment, 497, —symptoms of, 499

- Hip fractures, dorsal acetabular (dashboard fractures), 529  
Hirschsprung's disease sigmoido-rectomyotomy for, 492  
Histoplasmosis pulmonary, 219  
Hyaluronidase as therapy in chronic pleural empyema, 225  
Hydrocortisone acetate inhibitory effect on adhesions, 335  
effect on . . . . . effect on
- Hyperabduction syndrome pectoralis minor tenotomy and anterior scalenotomy in, 326  
Hyperparathyroidism acute primary, emergency parathyroidectomy for, 121  
Hypertension life expectancy of surgically and conservatively treated patients, 297, portal (see also Esophagus, varices), —diagnosis and treatment, 348, —portacaval and splenorenal shunts for (technics), 352, —surgical experiences in, 345, severe, follow up after sympathectomy, 295 f  
Hyperthyroidism radioiodine or surgery in 131  
Hypnosis and the anesthetist, 620, surgery under, 620  
Hypoglycemia with nonpancreatic tumors, 395  
Hypoparathyroidism postoperative, 118  
Hypophysectomy in advanced cancer, 152, in diabetic Kimmelstiel Wilson syndrome, 148, endocrine insufficiency after (in cancer patients), 154, in metastatic breast cancer, 148 ff, 152  
Hypotension controlled, blood loss and operative time with and without, 32, —during operation for coarctation of aorta, 294  
Hypothermia for amputation and tissue preservation, 519, controlled, in treatment of massive hemorrhage, 28, in heart surgery, 242 ff, hematologic changes in (dogs), 595 induction and control of, 43 local, favorable effect on surface bleeding (experimental), 72 partial hepatic resection under, 593, prolonged, experimental evaluation of, 30, sinoauricular node blockage for prevention of ventricular fibrilla-
- tion in, 594, in surgery, case analysis, 597  
Hypoxia perinatal, due to obstetric analgesia 541, role in hypothermic cardiac arrest in heart-lung preparation, 594
- I  
Ileitis regional cecal forms of, 471  
Infants (see Children)  
Inflammation destructive, injurious effects of cortisone on, 35  
Injuries arterial (from firearms), conservative treatment of, 292, from auto accidents, prevention of, 9, on farm, treatment of, 13, and ischemia, biochemical effects of 26, minor, treatment of, 16  
Instruments (see also specific devices) sterilization of, 10  
Intestine large, carcinoma of, relation to solitary polyps of colon and rectum (familial study), 469 —function after colectomy, 470 neomycin for preoperative preparation of, 80 obstruction, in aged, 460, small, Noble plication operation for recurring obstruction of, 450 ff, —recurrent obstruction due to adhesions, prevention, 454 —strangulation, antibiotic protection in, 456  
Ischemia experimental, biochemical effects of 26, peripheral arterial, management of pain in, 592  
Ivalon sponge in breast plastic and other soft tissue surgery, 138, tissue reactions to implants of, 37
- K  
Kidney artificial in treatment of surgical patients with anuria and uremia 24  
Kimmelstiel Wilson syndrome hypophysectomy in, 148
- L  
Labor chlorpromazine in management of, 539 f  
Legs by pass operation for arteriosclerotic occlusive disease of, 511  
Levallorphan effect on respiratory responses to CO<sub>2</sub> during narcotic and barbiturate depression in anesthesia, 548

Lipodystrophy isolated, form of mesenteric tumor, 337

Liver cirrhosis, with bleeding esophageal varices, shunting operations for, 351 ff; metastasis, from bronchial adenoma, 188; partial resection under hypothermia, feasibility of, 593; right lobectomy in children, 342; total right lobectomy for gallbladder cancer, 340 f

Lung carcinoma (see also Bronchus), —absence of increase in Soviet Union (?), 192, —alveolar cell, 216, —analysis of autopsy material of, 212, —cell types and histologic patterns in, 209, —in Copenhagen, 201; —death rates among nonsmokers and smokers, 191, —histologic types in diagnosis and prognosis of, 208, —histopathologic and cytologic correlation in, 190; —metastatic, resection for, 188; —physiologic aspects of, 213, —pneumonectomy vs lobectomy, 200, —pneumonectomy with intrapericardial dissection for, 203; —resection for, results, 200 ff, —and smoking, 94 ff, —sputum cytology for diagnosis of, 207, —surgical results in, 200, coccidioidomycosis of, 218, complications after thoracotomy, ale-vaire® for prevention of, 616, decortication, in tuberculous disease, 178, function tests with relation to anesthesia, 565

of pulmonary parenchyma, architectural reconstruction after, 165, —tracheostomy and prolonged artificial ventilation for ventilatory insufficiency after, 164, —for tuberculoma, 177

Lymphatic system superficial cutaneous (human), abnormalities of, 331

Lymphedema chronic, 328, post-mastectomy, 136, treatment of, 328 ff

## M

McWhirter treatment for breast cancer, evaluation, 140

Magnesium sulfate effect on al-

terations in renal dynamics induced by intravenous hemoglobin, 71

Marcumar prophylaxis for thromboembolism, 327

Mastectomy lymphedema following, 136, radical, fixation of skin flaps by subcutaneous sutures in, 137

Melanoma surgical treatment of, 102

Meperidine effect on respiration, 550

Mesotheliomas pleural, 232

Metabolism nitrogen, in surgical patient, 33

Middle lobe syndrome 173 ff

Mitral valve disease, reoperation for, 282, stenosis, commissurotomy for, 272, 276, 279, —evaluation by left heart catheterization, 269, —hemodynamics of left heart with reference to, 256, —pulmonary vessels in, 271, —valvuloplasty for, 278

Mondor's disease 324

Morphine effect on respiration in man, 550, increased intracranial pressure induced by, 543

Muscle relaxants anesthesia and facial paralysis, 572, results with intravenous gallamine triethiodide, 573

Myocardium infarction, postoperative, 289

## N

Necrosis traumatic fat, 18

Neomycin in preoperative preparation of bowel, 80

Newborn local anesthesia in, 591

Nisentil® effect on respiration, 550, and levallorphan (lorfan), effect on respiration during N-O-O<sub>2</sub> anesthesia, 547, for obstetric analgesia, avoidance of perinatal hypoxia with, 541

Nitrogen elimination, with semi-closed inhalers, factors influencing, 570, metabolism, in surgical patient, 33

Nitrogen mustard in treatment of serous effusions of neoplastic origin, 103

Noble plication operation for recurrent small bowel obstruction, 450 ff

Nucleic acid anabolism, relation to treatment of cancer, 104

Nutrition of cancer patients effect of tube feedings on, 55, surgical, principles of, 58  
Nylon tubes chemically treated, for arterial grafts, 300

## O

Oxygen and CO<sub>2</sub> tensions, use of 'arterialized' blood for determination of, 48; uptake, and lobar ventilation, influence of body position on, 161

## P

Pain control in cancer, 100, localized, deep procaine injection for, 47; neurophysiology of, 621, in peripheral arterial ischemia, management of, 592, subjective response and reaction to, 625

Pancreas annular, surgery of (technic), 395, carcinoma, aberrant, in jejunal diverticulum, 393; —pancreatoduodenectomy for, survival (over 5 years), 392, —resection, with two 5 year survivals, 382, disease, operative contrast visualization of, 388, islet cell tumor, ACTH for control of functioning metastases from, 394, surgery (1954 review from Mayo Clinic), 377

Pancreatitis acute, cholecystography during and immediately after, 364, —and acute cholecystitis, serum amylase test in differential diagnosis, 339, chronic re

Plasmin\* in prevention of adhesions, 336

Plastics tissue reaction to implantation of, 37

Pleura effusions, due to cancer, radiogold for, 107, —of neoplastic origin, nitrogen mustard for, 103, tumors, primary, 232

Pneumonectomy with intrapericardial dissection for bronchogenic carcinoma, 203, lobar alveolar gas concentration after, 162, osteoplastic wall thoracoplasty after, 228, radical, for bronchial carcinoma, 205, without thoracoplasty, in pulmonary tuberculosis, 183

Pneumoperitoneum in giant hernia management, 500

Polyps colonic and rectal, solitary, inherited tendency, 469

Pregnancy and cardiac surgery, 291

Procaine disappearance from plasma influence of anesthetic agents and ammonium chloride on, 618, injection (deep) for localized pain, 47

Proctitis factitial, clinical aspects, 490

Prothrombin activity inhibition with dextran, 68

Pyloric stenosis hypertrophic, congenital, familial occurrence of, 417, —clinical analysis of cases, 417, —in parent and child, 419

Pyribenzamine\* in reduction of nonhemolytic transfusion reactions, 64

## R

Radiochromium 51 in blood volume studies, application to anesthesiology, 601

Radiogold for effusions due to cancer, 107

Radioiodine or surgery in hyperthyroidism, 131

Radiotherapy with resection for bronchial carcinoma, 202

Rectum biopsy, in ulcerative colitis, 477, carcinoma, implantation of tumor cells in recurrence of, 487, —lateral spread, 486, —of rectosigmoid area, sphincter-preserving operation for, 484, —resection (anterior), 485 treatment of, 482, infactitial, 490

P.  
P.  
ogy of, 369

Paralysis facial, and muscle relaxant anesthesia 572

Paraplegia complication of spinal anesthesia, 583, 586

Parathyroidectomy emergency, for parathyroid crisis, 121

Pelvis exenteration (total) and wet colostomy, urinary tract after, 510

Pentobarbital for prevention of postanesthetic emetic symptoms, 625

Physical fitness index for evaluation of results of commissurotomy, 280

Pilonidal disease 4

- Refrigeration (see Hypothermia)  
 Regurgitation mechanism of, 399  
 Rehabilitation and surgery, 34  
 Relaxant drugs effects on vascular tone, using Sandison-Clark chambers, 607  
 Respiration (see also Ventilation) controlled, factors affecting pulmonary artery flow with, 554, depression, from narcotics and barbiturates, action of levallorphan on, 548; intermittent positive pressure apparatus, model lung for testing, 559, with misentil® and levallorphan (premixed solution) during N<sub>2</sub>O O<sub>2</sub> anesthesia, 547, physiology, in infants and young children under anesthesia, 564  
 Respiratory tract distribution and absorption of tobacco tar in, 196  
 Resuscitation in cardiac arrest, use of external electric pacemaker, 608  
 Roentgen therapy preoperative (high doses) with radical surgery for breast cancer, 134

## S

- Schreus apparatus for removal of acne scars and other cosmetic defects, 108  
 Schultz Dale test for detection of specific antigen in serums of patients with cancer, 85  
 Sedatives nonbarbiturate, evaluation of, 552  
 Serum amylase concentration in acute cholecystitis, 368, —in perforated gastroduodenal ulcer, 428, test, in acute abdominal disease, 49, 339  
 Shivering after thiopental and other anesthetic agents, 579  
 Shock secondary to limb clamping, efficacy of dextrans of different molecular weights in, 69, septic, 59, treatment of, 61  
 Shoulder-hand-finger syndrome 521  
 Sigmoidorectomyotomy for Hirschsprung's disease, 492  
 Sinus pilonidal, analysis of operations for, 495  
 Skin flaps, in radical mastectomy, subcutaneous sutures for fixation, 137, preparation for surgery, 10  
 Smoking and lung cancer, 94 ff, relation to lung cancer deaths, 191

- Spirometry in assessment of analgesia after abdominal surgery, 537  
 Splenectomy in patients with hemorrhagic tendency, 360, technic, 359  
 Sputum cancer cells in, 207  
 Stenosis (see also Pyloric stenosis) corrosive, esophageal, supra-aortic esophagogastric anastomosis without resection for, 415  
 Stor . . .  
 ra  
 —  
 sy  
 443, —chymotrypsin lavage for cytologic diagnosis of, 435 ff, —modified radical gastrectomy for, 441, —treated and untreated, natural history of survival in, 439, postanastomotic and postgastrectomy malfunctions, surgical management, 448, tumors, other than carcinoma, 444  
 Streptodornase clinical use of depolymerases of, 79  
 Surgery adrenal cortex insufficiency during, treatment, 618, blood and plasma in, 20, blood volume determinations in operative period, using radioactive iodinated serum albumin, 603, frozen section diagnosis in 88 f, under hypnosis, 620, increased aldosterone after, 27, and rehabilitation, 34, risk in patients with coronary heart disease, 23, thyroid activity during, 122  
 Sutures from ovine submucosa and bovine serosa, comparative antigenicity in guinea pigs of, 49  
 Sympathectomy chemical or surgical, evaluation of sympathetic activity after, 623, lumbodorsal, for hypertension (severe), results, 295 f  
 Sympathogalvanic reflex for determination of sympathetic activity after sympathectomy, 623

## T

- Tetanus current therapy of, 75, maximal curarization without anesthesia but with tracheostomy and artificial respiration in severe cases of, 76, prevention of, 73, toxoid antitoxin levels after inoculation and booster doses, 74

- Tetralogy of Fallot surgical correction of (follow-up), 284
- Thiopental and  $N_2O$  anesthesia hemodynamics during, 615, and thiethylal, in anesthesia, comparative study, 576; shivering following, 579
- Thoracic duct complete extirpation in primary benign tumor, 226, lesions, surgical management of, 332
- Thoracoplasty osteoplastic wall, after pneumonectomy, 228
- Thoracotomy alevure<sup>®</sup> for prevention of pulmonary complications after, 616, open, pulmonary ventilation during, 161
- Thromboembolism prophylaxis with anticoagulants (especially marcumar), 327
- Thrombophlebitis of superficial veins of breast and anterior chest wall (Mondor's disease), 324
- Thyroid gland activity, during operation, 122, carcinoma, in children, 115, 125, —conservative operations for, 126, —papillary, with and without cervical node involvement, 116, —pathologic physiology of, 117, —radical neck dissection for (pathologic evaluation), 128, —in San Francisco, 120
- Thyroiditis chronic, and Riedel's struma, cause and pathogenesis, 132
- Thyrotoxicosis thiouracil compounds and surgery in, 123
- Ti n  
d  
-  
er experimental results in, 35
- Tobacco tar distribution and absorption in respiratory tract, 196, production of skin cancer in different mouse strains with, 96
- Tonsillectomy in children endotracheal anesthesia for, 571
- Tracheostomy (see Tracheotomy)
- Tracheotomy and artificial respiration, 113, and prolonged artificial ventilation for ventilatory insufficiency after lung resection, 164, in tetanus, 75 f
- Transfusions blood and blood substitutes after controlled hypothermia, 28, —citrate (rapid and large), risk in hemorrhagic shock (dog), 22, —hazards of, 69, —and plasma, in surgical practice, 20, —total hemoglobin determination for evaluation in surgical patients, 22, intra-arterial, apparatus for, 63, reactions, agents causing, 69, —effect of  $MgSO_4$  on renal damage after, 71, —nonhemolytic, antihistamines for, 64
- Tuberculoma pulmonary resection for, 177
- Tuberculosis with bronchial carcinoma, 223, after gastrectomy, 449, pulmonary, bilateral resection in, 182, —pneumectomy without thoracoplasty, 183
- Tumors of bone, benign and malignant giant cell, 534, gastric, 444, glomus, case analysis, 532, human, heterologous growth in subcutaneous tissues of animal host, 92, mesenteric, isolated lipodystrophy, form of, 337, nonpancreatic hypoglycemia with, 395, turban 111
- U
- Ulcer, peptic duodenal, bleeding, suture control of, 434, —familial occurrence, 426, —physiologic concepts of vagotomy and gastroenterostomy, 432, gastroduodenal, perforated, serum amylase concentration in, 428, —simple suture in, 431, hemorrhage from, 423 ff, pain (acid induced), inhibition by local anesthetics, 621, perforated, nonoperative treatment of, 429, role of pyloric antrum in experimentally induced, 427, surgical results in 433
- Ultrasonic energy biophysical effects on cancer, 107
- Urinary tract after total pelvic exenteration and wet colostomy, 510
- V
- Valvotomy mitral follow up (3 years and over), 275
- Valvuloplasty for mitral stenosis, 278
- Varices esophageal, bleeding, surgery for, 411, sign of vascular malformation, 321
- Veins popliteal, division in femoral vein valve incompetence, portal, blood, bacteriologic of (in man), 350, —



347; *varicose*, and normal, comparative studies of blood of, 322, —results of surgery on, 322

Ventilation, blood gas changes dur-

ing for measuring maximal breathing capacity in individual lung, 163, factors affecting CO<sub>2</sub> elimination during closed system anesthesia, 556, insufficiency, after pulmonary resection, tracheostomy and prolonged artificial ventilation for, 164, lobar, and oxygen uptake (in man), influence of body

position on, 161, with partial re-breathing system, evaluation of, 557, after pneumonectomy, 162, *pulmonary*, during open thoracotomy, 161, —function tests for evaluation of anesthetic risk, 565

## W

Wounds healing, effect of previous level of protein feeding on (experimental), 56; *of heart*, long term follow-up, 241, —penetrating, treatment of, 240, incurred on farm, treatment of, 13, prevention of tetanus after, 73, surgical, asepsis and antiseptics of, 10



Braunwald, Eugene, 256  
 Brazell, Edward, 603  
 Brecher, Gerhard A., 554  
 Brewer, Lyman A., III, 332  
 Brewster, William R., Jr., 605  
 Briggs, Bernard D., 259  
 Brock, Russell, 205, 244, 275  
 Brockman, H. LeRoy, 240, 428  
 Brofman, B. L., 247  
 Bromage, P. R., 537  
 Bromley, L. L., 202  
 Bross, W., 225  
 Brossy, Jean-Jacques, 188  
 Brown, Allan S., 599  
 Brown, Elwyn S., 556, 557, 560  
 Bruce, Robert A., 280  
 Brunschwig, Alexander, 510  
 Buckwalter, Joseph A., 118  
 Bugden, Walter F., 409  
 Bulow, Knut, 271  
 Bunnell, Sterling, 522  
 Burford, Thomas H., 269  
 Burgerman, Arthur, 446  
 Burnett, W., 339  
 Busch, R. B., Jr., 587  
 Butcher, Harvey R., Jr., 331

## C

Cam, James C., 446  
 Calhoun, William K., 56  
 Calloway, Doris Howes, 56  
 Cameron, Angus L., 417  
 Campbell, Donald, 429  
 Campbell, Gilbert S., 610  
 Campbell, John M., 191  
 Campbell, Maurice, 275  
 Cannon, Jack A., 302  
 Cantrell, James R., 461  
 Carlens, Eric, 161  
 Case, Thomas C., 158  
 Cass, M. H., 43, 373  
 Cass, N. M., 607  
 Cattell, Richard B., 473  
 Chaet, Alfred B., 42  
 Chastrey, L. J., 111  
 Chambers, R. D., 607  
 Chapman, John S., 38  
 Chase, William W., 115  
 Chasen, William H., 74  
 Chesterman, J. T., 169  
 Christensen, Norman A., 497  
 Ciuti, Andrea, 395  
 Clagett, O. Theron, 170, 189  
 Clark, Dwight E., 131  
 Clark, J. B., 163  
 Clatworthy, H. William, Jr., 342, 393  
 Clement, Frederick L., 554  
 Cline, Frank, Jr., 162

Coakley, Charles S., 576  
 Coe, Walter S., 241  
 Cogswell, Howard D., 41  
 Cohen, Morley, 263, 264, 267  
 Cohn, Isidore, Jr., 80, 456  
 Colcock, Bentley P., 128, 473  
 Cole, William, 59  
 Collins, Donald C., 464  
 Collins, Vincent J., 571  
 Committee on Diabetes, Massachusetts Medical Society, 515  
 Conner, Eugene H., 601  
 Conrad, E. J., 55  
 Converse, J. Gerard, 549  
 Cooley, Denton A., 240  
 Cooley, Jack C., 170  
 Cooper, Philip, 48, 495  
 Costas-Durieux, Jaime, 250  
 Cotton, Bert H., 218  
 Crane, Jackson T., 337  
 Craver, Bradford N., 49  
 Craver, William L., 322  
 Crawford, E. Stanley, 511  
 Creech, Oscar, Jr., 309  
 Crile, George, Jr., 87, 126  
 Croninger, Adele B., 96  
 Crossman, Lyman Weeks, 519  
 Crowley, Lawrence G., 404  
 Curtis, George W., 593  
 Cutler, Sidney J., 81

## D

Dahlback, O., 304  
 Dahl-Iversen, E., 508  
 Dale, W. Andrew, 406  
 D'Allaines, F., 279  
 Daniel, William, 510  
 Dao, Thomas L.-Y., 502  
 Davies, Jack, 118  
 Davis, H. L., 19  
 Day, Sherman W., 77  
 DeBakey, Michael E., 240, 511  
 Decker, H. Ryerson, 216  
 Delarue, Jacques, 223  
 Delarue, Norman C., 155  
 Delmonico, J. Ernest, Jr., 409  
 DeLoach, A. W., 611  
 Demaria, William J. A., 71  
 Dennis, Clarence, 392  
 Denoix, Pierre F., 86  
 Denson, J. S., 587  
 Desprez, John D., 350  
 Deterling, Ralph A., Jr., 308  
 Detrick, Marion F., 291  
 DeWall, Richard A., 263  
 Dick, Walter, 524  
 Dickson, James F., III, 254  
 Dimitrov-Szokodi, Daniel, 172  
 Ditzler, John W., 32



Miller, George A, 166  
 Miller, Joseph M, 79  
 Miller, Robert, 286  
 Miller, Robert A, 284  
 Miller, Theodore R, 340, 341  
 Mills, Ernest L, 603  
 Minnis, J F, Jr, 379  
 Mithoefer, John C, 543  
 Moberg, Erik, 521  
 Mobley, Jack E, 497  
 Modlin, John J, 39  
 Mollaret, Pierre, 76  
 Moore, Lawrence T, 591  
 Moore, S W, 322  
 Morgan, C Naunton, 466  
 Morgenstern, Leon, 427  
 Morris, Kenneth N, 129  
 Morton, Douglas R, 405  
 Moscovitz, Howard L, 256  
 Motley, Hurley L, 565  
 Mowat, John H, 79  
 Muir, E G, 392, 482  
 Mulholland, John H, 386, 388  
 Muren, A, 304  
 Murphy, William R, 534  
 Murry, W E, 587  
 Mushin, William W, 573  
 Musselman, M M, 19  
 Myers, W P Laird, 151

## N

Nardi, C, 390  
 Nealon, Thomas F, Jr, 161  
 Ness, T D, 339  
 Neuman, Harold W, 227  
 New York State Society of Anesthesiologists, Anesthesia Study Committee, 589  
 Nguyen Huu, 292  
 Nicholas, Theodore H, 505  
 Niedner, Franz F, 347  
 Nieth, H, 297  
 Nilsson, L B, 154  
 Norden, G, 304  
 Norlander, Olof, 22  
 Norman, Leona R, 608  
 Norton, Harry I, 539  
 Nowill, W K, 542

## O

Oberhelman, Harry A, Jr, 424,

Orie, N G M, 246  
 Orkin, Louis R, 550  
 Osgood, Patricia F, 605  
 Osman, Kent, 136  
 Osmun, Paul M, 572  
 Ottosen, Pouf, 268  
 Oustrières, G, 167  
 Owen-Flood, Anthony, 620

## P

Paaby, H, 508  
 Pack, George T, 340, 341  
 Paillas, Jean, 223  
 Palmer, Walter L, 436  
 Paltia, V, 357  
 Pangman, W John, II, 138  
 Papper, E M, 576  
 Pareira, M D, 55  
 Parkins, William M, 61  
 Parrish, Charles M, 352  
 Patterson, Howard A, 478  
 Paul Milton H, 608  
 Paulino, Fernando, 175  
 Paulsen, George A, 218  
 Payne, J P, 586  
 Payne, J Thomas, 57  
 Pearson, O H, 152  
 Pearson, Olof H, 150, 151  
 Pecora, David V, 495  
 Peereboom, Gerrit, 262  
 Pender, John W, 600  
 Perasalo, O, 403  
 Peterson, O S, Jr, 603  
 Peterson, Ralph E, 507  
 Pfeffer, K H, 297  
 Phan-Ha-Thanh, 292  
 Phillips, John W, 487  
 Pickrell, Kenneth, 532  
 Pinc Roger D, 313  
 Pleticka, Sylvia, 436  
 Pollack, Robert S, 102  
 Pollard H M, 439  
 Potts, Willis J, 284  
 Poulsen, Thue, 201  
 Prendergast, Paul, 30  
 Price, Henry L, 601  
 Price, Joyce E, 161  
 Priestley, James T, 377  
 Proger, Samuel, 23  
 Protheroe, R H B, 477  
 Puckett, Thomas F, 219



Miller, George A, 166  
 Miller, Joseph M, 79  
 Miller, Robert, 286  
 Miller, Robert A, 284  
 Miller, Theodore R, 340, 341  
 Mills, Ernest L, 603  
 Minnis, J F, Jr, 379  
 Mithoefer, John C, 543  
 Moberg, Erik, 521  
 Mobley, Jack E, 497  
 Modlin, John J, 39  
 Mollaret, Pierre, 76  
 Moore, Lawrence T, 591  
 Moore, S W, 322  
 Morgan, C Naunton, 466  
 Morgenstern, Leon, 427  
 Morris, Kenneth N, 129  
 Morton, Douglas R, 405  
 Moscovitz, Howard L, 256  
 Motley, Hurley L, 565  
 Mowat, John H, 79  
 Muir, E G, 392, 482  
 Mulholland, John H, 386, 388  
 Muren, A, 304  
 Murphy, William R, 534  
 Murry, W E, 587  
 Mushin, William W, 573  
 Musselman, M M, 19  
 Myers, W P Laird, 151

## N

Nardt, C, 390  
 Nealon, Thomas F, Jr, 161  
 Ness, T D, 339  
 Neuman, Harold W, 227  
 New York State Society of Anesthesiologists, Anesthesia Study Committee, 589  
 Nguyen-Huu, 292  
 Nicholas, Theodore H, 505  
 Niedner, Franz F, 347  
 Nieth, H, 297  
 Nilsson, L B, 154  
 Norden, G, 304  
 Norlander, Olof, 22  
 Norman, Leona R, 608  
 Norton, Harry I, 539  
 Nowill, W K, 542

## O

Oberhelman, Harry A, Jr, 424, 432  
 Ogilvie, Heneage, 376  
 Olcott, Charles T, 209  
 Olivecrona, H, 148, 154  
 Olivier, Cl, 321  
 Olney, John M, 507  
 Olsen, Arthur M, 170  
 Olsen, Clarence W, 578

Orie, N G M, 246  
 Orkin, Louis R, 550  
 Osgood, Patricia F, 605  
 Osman, Kent, 136  
 Osmun, Paul M, 572  
 Ottosen, Poul, 268  
 Oustrières, G, 167  
 Owen-Flood, Anthony, 620

## P

Paaby, H, 508  
 Pack, George T, 340, 341  
 Paillas, Jean, 223  
 Palmer, Walter L, 436  
 Paltia, V, 357  
 Pangman, W John, II, 138  
 Papper, E M, 576  
 Pareira, M D, 55  
 Parkins, William M, 61  
 Parrish, Charles M, 352  
 Patterson, Howard A, 478  
 Paul, Milton H, 608  
 Paulino, Fernando, 175  
 Paulsen, George A, 218  
 Payne, J P, 586  
 Payne, J Thomas, 57  
 Pearson, O H, 152  
 Pearson, Olof H, 150, 151  
 Pecora, David V, 495  
 Peereboom, Gerrit, 262  
 Pender, John W, 600  
 Perasalo, O, 403  
 Peterson, O S, Jr, 603  
 Peterson, Ralph E, 507  
 Pfeffer, K H, 297  
 Phan-Ha-Thanh, 292  
 Phillips, John W, 487  
 Pickrell, Kenneth, 532  
 Pinc, Roger D, 313  
 Pleticka, Sylvia, 436  
 Pollack, Robert S, 102  
 Pollard H M, 439  
 Potts, Willis J, 284  
 Poulsen, Thue, 201  
 Prendergast, Paul, 30  
 Price, Henry L, 601  
 Price, Joyce E, 161  
 Priestley, James T, 377  
 Proger, Samuel, 23  
 Protheroe, R H B, 477  
 Puckett, Thomas F, 219

## Q

Qvigstad, G, 123

## R

Randall, Henry T, 341  
 Rao, K V S, 616  
 Ravitch, Mark M, 256

Ray, B. S., 152  
 Read, Raymond C., 263  
 Reed, Robert, 18  
 Reichert, Frederick Leet, 47  
 Rentzhog, Uno, 363  
 Reynolds, John L., 394  
 Rhoads, C. P., 104  
 Rhoads, Jonathan L., 61  
 Riberi, A., 594  
 Richards, Paul G., 121  
 Richards, Ralph C., 469  
 Rickards, A. G., 583  
 Ridley, Roger W., 615  
 Riker, William L., 286  
 Rios Mozo, M., 402  
 Roberts, Brooke, 18  
 Roberts, Kathleen E., 341  
 Robson, B., 373  
 Roegel, L., 165  
 Rogers, C. S., 159  
 Rosenbaum, Paul J., 122  
 Ross, D. N., 244  
 Rovenstine, L. A., 550  
 Rowlands, B. C., 80  
 Ruben, J. Eugene, 616  
 Rubin, Cyrus E., 435  
 Ruhenstroth, G., 35  
 Ruiter, D., 180  
 Rule, James H., 131  
 Rundle, F. F., 373  
 Russ, Clam, 30

## S

Sadove, Max S., 576  
 Saegesser, Max, 492  
 Saichek, Robert P., 289  
 Samson, Paul C., 234  
 Samuel, Eric, 371  
 Sancetta, S. M., 587  
 Sandblom, Ph., 304  
 Sanders, George B., 458  
 Sandweiss, David J., 365  
 Sapin, Samuel O., 256  
 Saubier, E. C., 177, 200  
 Sauvage, Lester R., 313  
 Savage, T., 178  
 Sawyer, C. Douglas, 379  
 Scanlon, Edward F., 405  
 Schapiro, Herbert, 621  
 Schatten, William E., 350  
 Schirmer, Jacob F., 345  
 Schlosser, Ralph J., 298  
 Schmidt, Erwin R., 489  
 Schmidt-Ueberrichter, E., 159  
 Schneider, H., 297  
 Schonbauer, L., 159  
 Schrire, T., 441  
 Schultz, Jeppe, 268  
 Schuster, Norah, 207

Schwimgt, E., 431  
 Schweizer, Olga, 619  
 Scorer, Eileen M. C., 80  
 Sears, W. Gordon, 552  
 Sebeck, Roy, 513  
 Secher, Ole, 294  
 Sedgwick, Cornelius E., 352  
 Seegers, Walter H., 68  
 Seeley, Sam F., 429  
 Sekkenes, J., 154  
 Sellers, A. M., 296  
 Selman, M. W., 253  
 Senning, Ake, 22  
 Sewell, W. H., 529  
 Sewell, William R., 49  
 Shanon, D. B., 438  
 Shapiro, Shepard, 50  
 Shea, Patrick C., Jr., 367  
 Shedd, Donald P., 404  
 Sheldon, David B., 259  
 Sheridan, C. A., 568  
 Sherman, Charles D., Jr., 406  
 Shumacher, H. B., Jr., 594  
 Shumway, Norman E., 242  
 Shurer, Julian G., Jr., 126  
 Siker, Ephraim S., 546  
 Silvis, Richard S., 395  
 Simon, Daniel S., 395  
 Simon, Norman, 107  
 Singleton, A. O., Jr., 611  
 Sjogren, B., 154  
 Sjolm, Knud-Erik, 89  
 Slater, H. M., 568  
 Slaughter, Danely P., 100  
 Smith, Gordon K., 452  
 Smith, Lorraine C., 69  
 Smith, Louis J., 540  
 Smith, Ralph E., 282  
 Smith, Ranson L., 603  
 Smith, Robert M., 579  
 Smith, Scott M., 576  
 Snyder, Howard E., 13  
 Söndergaard, Tyge, 268  
 Sones, F. Mason, Jr., 262  
 Soper, Robert T., 118  
 Sørensen, B., 508  
 Sørensen, Hans Rahbek, 201  
 Soulier, J. P., 360  
 Southwick, Harry W., 100  
 Spalding, J. M. K., 559  
 Spear, Harold C., 173  
 Spjut, Harlan J., 190  
 Sprafka, Joseph L., 282  
 Strabins, Samuel J., 406  
 Stafford, Edward S., 46  
 Stamer, John P., 241  
 Starkey, George W. B.,  
 State, David, 427  
 Steinberg, M. E., 448



## INDEX TO AUTHORS

Steiner, H, 463  
 Stemmer, Edward A, 20  
 Stephen, C R, 542  
 Stephen, C Ronald, 64  
 Stocks, Percy, 191  
 Stone, Peter W, 326  
 Storaasli, John P, 103  
 Stout, Arthur Purdy, 88  
 Straith, Richard E, 591  
 Stroud, M W, 3rd, 567  
 Stuckey, Douglas, 239  
 Sugar, Benjamin, 421  
 Sulamaa, M, 357  
 Summers, W, 506  
 Surmonte, John A, 79  
 Swan, Henry, 243, 597  
 Swerdlow, Mark, 545  
 Swiss, L D, 618  
 Symmers, W St C, 90  
 Szur, Leon, 202

## T

Takimura, Y, 362  
 Tapp, James S, 300  
 Teasley, Jack L, 591  
 Tandler, Morton J, 395  
 Ter Brugge, R, 246  
 Tesluk, Henry, 459  
 Therkelsen, Frederik, 294  
 Thomas, George J, 576  
 Tobiasen, Grete, 232  
 Tobiasen, T, 508  
 Toft, Gudmund, 208  
 Toolan, Helene Wallace, 92  
 Touroff, Arthur S W, 305  
 Tovell, Ralph M, 576  
 Traylor, F, 506  
 Treves, Norman, 135  
 Trout, Hugh H, Jr, 147  
 Truelove, S C, 476  
 Turnock, Dorothy, 26

## V

Valiente, Miguel A, 472  
 Vanamee, Parker, 341  
 Vandam, Leroy D, 580  
 van den Brenk, H A S, 607  
 Varco Richard L, 263, 264, 267,  
 392  
 Vars, Harry M, 61  
 Vaun, William S, 61  
 Verneil G, 167  
 Viguie, Roger, 471  
 Villalobos, Julio J, 596  
 Virtue, Robert W, 243, 597  
 von Brandis, H J, 327  
 von Euler, U, 154

## W

Wagner, J Huber, 531  
 Walford, Alfred S H, 113  
 Walker, F, 260  
 Walker, John M, 405  
 Wallace, Robert M, 138  
 Wallen, Per, 336  
 Waller, Ake, 529  
 Walters, Waltrmann, 372, 374, 377  
 Wangenstein, Owen H, 470  
 Wantz, George, 460  
 Warden, Herbert E, 263, 264, 267  
 Warren, Kenneth W, 384  
 Waschewsky, H J, 154  
 Wasmuth, Carl E, 603  
 Wasserman, Fred, 289  
 Waterman, David H, 234  
 Watson, A B, 526  
 Watson, William L, 405  
 Watt, William V, 147  
 Waugh, John M, 377  
 Weksnar, John F, 75  
 Werner, Robert S, 48  
 Weingarten, Maxwell, 539  
 Weisberger, Austin S, 103  
 Weiss, A G, 431  
 Weisschedel, E, 462  
 Welch, Claude E, 420, 480  
 Wenger, Don S, 9  
 Wesolowski, Sigmund A, 313  
 West, Charles D, 150, 151, 152  
 White, C W, Jr, 618  
 White, Harvey, 284  
 White, Paul D, 295  
 White, Raleigh R, 454  
 Whytehead, L L, 205  
 Wickbom, Ingmar G, 363  
 Wierman, William H, 203  
 Wilde, Ralph, 30  
 William, Vallee L, 72  
 Williams, Edward K, 558  
 Williams, Roger D, 58  
 Wilson, Edward, 485  
 Wilson, Hugh E, III, 254  
 Wilson Roger H L, 213  
 Winblad, Sten, 271  
 Winship, Theodore, 115  
 Winslow, William Allen, 99  
 Witt, Raymond, 368  
 Witts, L J, 476  
 Wolf, E, 165  
 Wood, David A, 213  
 Wood, Earl H, 615  
 Wood, Earl W, 600  
 Woodward, Edward R, 621  
 Woolf, Charles, 469

Woolner, Lewis B , 125  
Worn, H , 222  
Wright, J T , 426  
Wulff, Helge B , 271  
Wylie, R G , 43  
Wynder, Ernest L., 94, 96

## Y

Young, S A , 559  
Ytrehus, O , 123

## Z

Zachariae, Lis, 335  
Zak, Frederick G , 393  
Zech, Ralph K., 298  
Ziegler, Newell R , 263, 267  
Zimmerman, Herbert B , 269  
Zintel, H A , 296  
Zintel, Harold A , 10  
Zoll, Paul M , 608  
Zollinger, Robert M , 58  
Zweifach, B W , 604



